



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

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MEMORANDUM

DATE: TBD, 2018

SUBJECT: Final Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam

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This memo transmits the Environmental Fate and Effects Division's Final Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam. This assessment updates the Preliminary Bee Risk Assessment (1/5/2017, DP 437097) and incorporates additional information, submitted to the Environmental Protection Agency after completion of the preliminary document, for assessing the risks of agricultural and non-agricultural uses of clothianidin and thiamethoxam to bees. Where appropriate, this assessment incorporates comments received during the public comment period on the preliminary risk assessment document.

Major updates that have been made to this final assessment include the following:

- Two repeat sucrose colony feeding studies (one for clothianidin and one for thiamethoxam) were incorporated along with associated updated endpoints, as appropriate.
- A pilot pollen colony feeding study conducted with clothianidin was incorporated.
- The methodology to assess clothianidin and thiamethoxam residues in pollen was revised. The new methodology replaces the previous "bee bread" methodology and combines residues from nectar and pollen into a total dietary dose.
- Additional residue study data were considered, which provide residues of clothianidin and thiamethoxam in nectar, pollen, leaves and various other plant matrices for registered crop uses.
- A residue bridging strategy has been employed to reach refined risk conclusions and to bridge existing residue data for individual crop / application method / chemical data points to fill in the gaps for crops that don't have residue data available.
- This document includes risk conclusions for non-agricultural use sites, which were not included in the Preliminary Bee Risk Assessment.

Risk conclusions for all other non-bee taxa from exposure to clothianidin and thiamethoxam were included in separate preliminary risk assessments¹ from the bee assessment. Updates to the non-bee taxa risk assessments and response to public comments received for those documents are addressed separately.

¹ Clothianidin Preliminary Aquatic and Non-Pollinator Terrestrial Risk Assessment to Support Registration Review (11/27/2017, DP 439290)

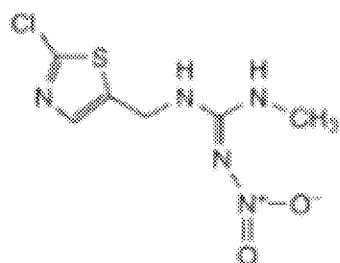
Thiamethoxam Preliminary Aquatic and Non-Pollinator Terrestrial Risk Assessment to Support Registration Review (11/29/2017, DP 439307)



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Final Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam

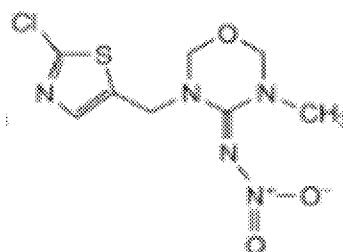


Clothianidin

PC Code: 044309

IUPAC: (E)-1-(2-Chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine

CAS: 210880-92-5 (previously 205510-53-8)



Thiamethoxam

PC code: 060109

IUPAC: 3-(2-Chloro-thiazolyl-5-ylmethyl)-5-methyl-[1,3,5]oxadiazinan-4-ylidene-N-nitroamine

CAS: 153719-23-4

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- 1 Tier II pollen and nectar exposure method
- 2 Residue bridging analysis for foliar and soil applications to agricultural uses
- 3 Residue bridging analysis for non-agricultural uses
- 4 Residue bridging analysis for seed treatment applications to agricultural uses

1 Executive Summary

1.1 Overview

Scope of the Assessment

The purpose of this assessment is to determine potential risks of thiamethoxam and clothianidin use to honey bees (*Apis mellifera*). Additionally, consideration of potential risk to other non-*Apis* bees, including bumble bees (*Bombus sp.*) was also evaluated. In 2017, EPA issued its Preliminary Ecological Risk Assessment for bees that evaluated agricultural uses of clothianidin and thiamethoxam. Following the receipt of public comments on the 2017 Preliminary Pollinator Risk Assessment and additional data, the Agency has issued this Final Bee Risk Assessment for clothianidin and thiamethoxam which: (i) incorporates modifications based on public comments where appropriate; (ii) includes additional exposure and effects data the Agency received since the preliminary assessment; (iii) assesses the potential risks associated with registered agriculture and non-agricultural uses of these chemicals to bees; and iv) incorporate and describe new pollen method and bridging strategy.

These two chemicals are again assessed in one document because 1) although clothianidin is a registered active ingredient, the compound is a major degradate of thiamethoxam; 2) the toxic effects and the concentrations at which they occur for these two chemicals are similar for bees; and, 3) their use patterns are similar. Clothianidin is observed as a major degradate of thiamethoxam in many fate studies and was detected in pollen and nectar residue studies. In this assessment, exposure and effects are expressed as “clothianidin equivalents” (c.e.), where thiamethoxam concentrations are converted using the molecular weight ratio of clothianidin to thiamethoxam (*i.e.*, ratio=0.856)². Both chemicals are assessed here individually, with independent risk conclusion for each chemical based on the available data and analysis.

This assessment follows the methodology outlined in the 2014 Guidance for assessing pesticide risks to bees³ and uses a tiered assessment approach. Tier 1 evaluates risks to individual bees based on Risk Quotients (RQs) calculated using laboratory toxicity data and default modeled (BeeREX) exposure estimates. Where Tier I RQs exceed the Agency’s level of concern (LOC), a refined Tier I assessment is conducted using available empirical (measured) residues of clothianidin/thiamethoxam (expressed as c.e.) in pollen and/or nectar of specific crops to replace model estimates of exposure. These empirical values are compared to the same laboratory-based toxicity endpoints. Where risks of concern are still identified at the refined Tier I level, a Tier II assessment is conducted. At the Tier II level residues in pollen and nectar are either 1) used from available empirical measurements (as in the refined Tier I analysis) or 2) used from other neonicotinoids (*i.e.*, bridged) and compared to colony-level effect endpoints from honey bee colonies exposed to thiamethoxam and/or clothianidin. To evaluate the potential for colony-level effects (*i.e.*, Tier II analysis), this assessment uses a colony dietary⁴ exposure approach by combining measured residues in both pollen and nectar and adjusting for relative consumption of each matrix to provide a dietary concentration that can be compared back to Tier II feeding studies. Other

² This was done in the Preliminary Pollinator Assessment and is carried through in this Assessment for consistency.

³ https://www.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf

⁴ The previous assessment considered exposure from pollen (via bee bread) and nectar separately.

relevant information is also considered in this assessment, such as reported incidents involving bees and toxicity information for other species of bees.

Use Profile

Clothianidin and thiamethoxam may be applied to crops via a variety of methods including aerial and ground (foliar) sprays, soil treatment (*e.g.*, drench), chemigation (*e.g.*, soil incorporation or foliar), and as a seed treatment. Clothianidin and thiamethoxam are used on a wide array of agricultural crops, including (but not limited to): root and tuber vegetables, leafy vegetables, brassica, cucurbits, fruiting vegetables, cereal grains, citrus fruit, pome fruit, stone fruit, berries, tree nuts, beans and other legumes, herbs, oilseed crops (*e.g.*, canola, cotton), and tobacco. There are currently 45 registered Section 3 end-use products for clothianidin and 78 end-use products for thiamethoxam. When considering the same uses, single maximum application rates for clothianidin for foliar sprays are generally higher than those allowed for thiamethoxam. Maximum single application rates for clothianidin are 0.1 or 0.2 lb c.e./A, for most crops; whereas, maximum single application rates for thiamethoxam are 0.040, 0.054 or 0.074 lb c.e./A.

According to the most recent usage reports provided by the Biological and Economic Analysis Division (BEAD) as of December 30, 2015, the majority of thiamethoxam used on agricultural crops is applied to soybeans (300,000 lbs/year on seeds), corn (300,000 lbs/year on seeds) and cotton (160,000 lbs/year on seeds and plants). The vast majority of clothianidin (1,400,000 lbs/year) is applied to corn (as a seed treatment). For soybean, an estimated annual average of 15% of the total crop planted in the US is seed treated with thiamethoxam, and <2.5% is treated with clothianidin (with less than <2.5 % also the maximum for clothianidin and 25% for thiamethoxam in any given year). For corn, an estimated annual average of 45% of the total crop planted in the US is treated with clothianidin, and 25% is treated with thiamethoxam (maximum of 65% for clothianidin and 45% for thiamethoxam in any given year). For cotton, an estimated annual average of 10% of the total crop planted in the US is seed treated with thiamethoxam, and <2.5% is treated with clothianidin (with less than <2.5 % also the maximum for clothianidin and 45% for thiamethoxam in any given year).

Clothianidin and thiamethoxam also have non-agricultural uses including turf, tree plantations, poultry houses, ornamental plants and in and around domestic and commercial buildings.

The sections below summarize the risk conclusions and incorporates several lines of evidence including results from the Tier I and II assessments as well as other considerations including incidents reports.

1.2 Risk Conclusions Summary: honey bees

Tables 1.1 and 1.2 summarize the risk conclusions for honey bee colonies associated with each crop or crop group⁵ for which clothianidin and thiamethoxam (respectively) are registered. Conclusions are for on-field exposures and are expressed as red text indicate uses of clothianidin and thiamethoxam which pose risks to bees. Green text indicates cases where the likelihood of adverse effects on bees from a particular use is considered low. For those uses where there are risk concerns for colony level effects, the weight of evidence supporting the risk conclusion is characterized as either strongest, moderate or weakest.

⁵ Crops groups are codified in 40 CFR 180.41 and can be found here: <https://www.ir4project.org/crop-grouping/>

Multiple lines of evidence were considered to evaluate risk conclusions and the characterization of the strength of the weight of evidence for risk calls characterized as “strongest”, includes factors such as: multiple residue values (total food) above colony level NOAEC and LOAEC, estimated median, 70th and 90th percentile residues above colony level NOAEC and LOAEC, duration of residues above colony level endpoints on the order of weeks, magnitude of residues relative to endpoints suggests that substantial dilution of residues from uncontaminated food sources would be needed to prevent colony-level effects, and empirical residues exceeding colony level endpoints at multiple sites and/or crops. Conversely, crop group weight of evidence risk conclusions that are deemed “weakest” are those characterized by few and/or marginal exceedances of colony level effects endpoints or where confidence in bridging relationships was relatively lower (*e.g.* bridging data from outside of a crop group). The majority of the analysis is based on three robust colony feeding studies (Tier II) submitted for clothianidin and thiamethoxam and the available data regarding residues in bee-relevant floral matrices. Other supplemental/qualitative semi-field (Tier II) studies and full field (Tier III) studies were also considered as lines of evidence when available for a given use. Reported incidents were also considered.

Robust residue data sets are available for foliar applications to the following bee attractive crops and crop groups: cotton, cucurbits, citrus, stone fruit, pome fruit, tree nuts, berries, soybeans and ornamentals. Robust residue data sets are available for soil applications to cucurbits, citrus, and berries. In general, residues from soil treatments are lower than those from foliar treatments and seed treatment residues are lower than those from soil applications. Residues for cucurbits were considered as surrogates for other non-woody crops with limited or no residue data (*e.g.*, root and tubers, fruiting vegetables, mint), though this was considered a significant source of uncertainty (**Attachment 3**) and resulted in “weakest” risk calls. Taxonomic relationships were also considered, as appropriate, for bridging available residues from one crop group to related taxa in a separate crop group (*e.g.* cotton residues in the oilseed group were used as a surrogate for okra and roselle residues in the fruiting vegetable group, where all three are in the Malvaceae family). Residues for stone fruit, pome fruit and citrus are used for other woody crops (*e.g.*, tree nuts, tropical fruits).

In general, if a crop is attractive to bees and there is potential for exposure, colony level on-field risks to honey bees is expected from pre-bloom, foliar applications. The on-field risk from soil applications varies by use. In general, soil treatments pose a low risk; however, there are some limited exceptions (*e.g.* ornamentals, citrus). For uses with risk, the weight of evidence is characterized in terms of its robustness.

Uses with Low On-Field Risk:

This assessment concludes that clothianidin and thiamethoxam application to the following crops and crop groups pose a low risk to honey bees because they are harvested prior to bloom (according to USDA 2017) and have limited on-field exposure to bees: bulb, leafy and brassica leafy vegetables; artichoke and tobacco. Therefore, any type of applications (*i.e.*, foliar, soil or seed) to these crops would pose a low on-field risk to bees. For these crops, one exception would be cases where the crop is grown for seed, thus, the crop would not be harvested prior to bloom. Although clothianidin and/or thiamethoxam may be applied to crops grown for seed, the spatial footprint for these uses is expected to be limited due to low pounds applied and specific geographic areas where crops are grown for seed.

This assessment concludes that the following crops and crop groups pose a low risk to honey bees because they are not attractive to honey bees (according to USDA 2017) and have limited on-field exposure to honey bees: root and tuber vegetables (except sweet potato, Jerusalem artichoke, edible

burdock, dasheen and horseradish), fruiting vegetables (except roselle, okra, chilies and peppers). Therefore, any type of applications (*i.e.*, foliar, soil or seed) to these crops would pose a low on-field risk to honey bees.

For crops where clothianidin or thiamethoxam are applied as seed treatment, there is a low risk from exposures of clothianidin and thiamethoxam to honey bees. These conclusions are based on available empirical residue data for seed treated crops (*i.e.*, corn, cotton, canola and soybeans) and bridging to other crops receiving seed treatments. Although the default BeeREX RQs are above LOCs, the majority of refined RQs (with empirical residues) are below LOCs. For clothianidin, the following uses had refined Tier I RQs above the LOCs for adult bees: canola, cereal grains, legumes, sorghum and soybeans. When residues were compared to the Tier II honey bee colony endpoints, residues were all below the NOAEC, indicating low risk of colony level effects. For thiamethoxam, the following uses had refined Tier 1 RQs above the LOC for adult bees: beans, cucurbits, legumes, lentils, peanuts, peas, sorghum, soybeans and sunflower. All uses had residues below the clothianidin and thiamethoxam colony level NOAEC (both are considered because both chemicals are part of thiamethoxam's residues of concern), except for cucurbits. The weight of evidence indicates a low risk from thiamethoxam seed treatments to cucurbits. In summary, a low risk conclusion is made for on field exposures associated with all clothianidin and thiamethoxam seed treatment uses, except clothianidin applications to turmeric seed pieces (discussed below).

Low risk conclusions are also made for several foliar or soil uses because residues were below colony level endpoints. This applies to the following crops (or groups):

- Foliar applications of clothianidin and thiamethoxam to soybeans;
- Foliar, post-bloom applications of clothianidin and thiamethoxam to orchard crops;
- Foliar and soil, post-bloom applications of clothianidin and thiamethoxam to berries;
- Soil, pre-bloom applications of clothianidin to grapes.

Uses With On-Field Risk and Strongest Evidence of Risk:

The uses listed in this section are identified as posing a risk to honey bee colonies with strong weight of evidence. Lines of evidence indicating A strong evidence of risk is are considered where many measured residues for the crop of interest exceed both the colony level LOAEC and NOAEC for a relatively long duration (*e.g.*, several weeks), where residues are an order of magnitude above CFS endpoints (indicating that only a small fraction of the honey bee colony's nectar and pollen need to be from treated fields) and/or where multiple locations in the residue trials and/or multiple crops within the crop group yielded residues above CFS endpoints. In addition, incident reports of bee kills (*i.e.*, for clothianidin use on cotton; for thiamethoxam use in orchards) may provide additional lines of evidence for a strong evidence of risk conclusion. The following uses represent a risk to honey bee colonies and have the strongest weights of evidence.

- For Clothianidin:
 - o Foliar applications to cotton;
 - o Foliar applications to cucurbits;
 - o Foliar, pre-bloom applications to grapes.
 - o Foliar and soil applications to ornamentals
- For Thiamethoxam:
 - o Foliar applications to cotton;
 - o Foliar applications to cucurbits;

- Foliar, pre-bloom applications to orchard crops (*i.e.*, citrus; pome, stone and tropical fruits; tree nuts);
- Soil, pre-bloom applications to citrus;
- Foliar and soil, pre-bloom applications to berries; and
- Foliar applications to honey bee attractive fruiting vegetables (*i.e.*, okra, roselle, chilis and peppers).
- Foliar and soil applications to ornamentals

Uses with On Field Risk and Moderate Evidence of Risk:

The uses listed in this section are identified as posing a risk to honey bee colonies. These uses have a moderate weight of evidence, due to varying reasons (*e.g.*, not all lines of evidence suggest risk, or there are some uncertainties associated with the data that can influence the risk conclusion). Similar to above, multiple lines of evidence were considered to evaluate risk conclusions, including: multiple residue values (total food) above colony level NOAEC and LOAEC, duration of residues above colony level endpoints on the order of weeks, magnitude of residues relative to endpoints and incident reports.

The following uses represent a risk to honey bee colonies and have moderate weights of evidence:

- Clothianidin and Thiamethoxam:
 - Soil, post-bloom applications to citrus;
 - Soil applications to cucurbits;
 - Foliar applications to residential lawns; and
 - Foliar and soil applications to ornamentals.
- Thiamethoxam only:
 - Soil applications to honey bee attractive fruiting vegetables; and
 - Soil applications to cucurbits.

Uses with On Field Risk and Weakest Evidence of Risk:

The uses listed in this section as posing a risk to honey bees but have the weakest evidence of risk. These are cases where there is evidence to suggest colony level effects; however, it is not well supported by measured residue data (*e.g.* only a few (out of many) residue samples exceed colony level endpoints or where no residues for the crop group are available and significant uncertainties exist with the bridging of other available data to these uses. The following uses represent a risk to honey bee colonies and have the weakest weights of evidence:

- Clothianidin
 - Foliar and soil applications to honey bee attractive root and tuber crops (*i.e.*, sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish); and
 - Seed treatment to turmeric.
- Thiamethoxam
 - Foliar and soil applications to honey bee attractive root and tuber crops;
 - Post-bloom soil applications to citrus
 - Foliar applications to mint.

For thiamethoxam applications (foliar) to mint and for clothianidin seed treatments to turmeric (seed pieces), the evidence is considered weakest because risk findings rely exclusively on residue data that are extrapolated (bridged) from other neonicotinoids or different crop groups where the influence of crop on the magnitude of the residue is highly uncertain.

For clothianidin and thiamethoxam applications to honey bee attractive root and tuber crops, the evidence is considered weakest because of the following. Residue data are available for potato pollen for clothianidin; however, this crop does not produce nectar, but other crops in the group do (*e.g.*, sweet potatoes). Residues in potato (*Solanum tuberosum*) pollen are below the colony level endpoints; however, it cannot be concluded that honey bee attractive root and tuber crops pose a low risk because there are no residue data for nectar. When considering residue data for other field crops (*e.g.*, cotton, cucurbits), foliar and soil applications result in residues in nectar that are above the colony level endpoints. This suggests a potential concern. Information provided by BEAD suggests that several of these honey bee attractive root and tuber crops are cultivated primarily through their roots and not through setting seed, however without further information on the timing of cultivation relative to bloom periods, honey bee exposure cannot be precluded.

Off Site Risk Conclusions:

Based on a Tier I analysis, for foliar applications, off-field dietary risks to individual bees exposed to spray drift extend 1000 feet from the edge of the treated field. There is uncertainty in this conclusion which includes: assumption of available attractive forage off field, individual level toxicity data, BeeREX default estimates for residues, and AgDRIFT™ modeling.

Soil applications are assumed to have a low off-field risk because of low potential to drift.

In regard to seed treatments, there are risk concerns for potential off-site transport of contaminated dust at the time of planting. This concern is supported by multiple bee kill incidents for both clothianidin and thiamethoxam that are associated with the planting of treated seed, in particular corn.

Additionally, soil amendments of clothianidin-treated poultry litter (from the use in poultry houses) also pose a risk when applied to fields with honey bee attractive plants (*e.g.*, pasture).

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Summary of on-field risk findings for honey bee colonies (*Apis mellifera*) for the registered use patterns of clothianidin.

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data used quantitatively ⁸	Individual Bee (Tier I) Risk		Honey Bee Colony Risk (Tier II)?	Risk Conclusions ^{2,3}
					On Field (Default)	On Field (Refined)		
1	Root and Tuber Vegetables	Yes ⁵	Foliar	No	Yes	Yes	Yes	RISK: Weakest
			Soil	No	Yes	Yes	Yes	RISK: Weakest
			Seed	No	Yes	NA	No (except turmeric)	RISK: Weakest Turmeric only
		No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed	No	NA ³	NA	NA	LOW ⁴
3	Bulb Vegetables	No	Seed	No	NA ³	NA	NA	LOW ⁴
4	Leafy Vegetables	No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed	No	NA ³	NA	NA	LOW ⁴
5	Brassica Leafy Vegetables	No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed	No	NA ³	NA	NA	LOW ⁴
6	Legume Vegetables	Yes	Foliar (Soybean-only)	Soybean (I) (T)	Yes	NA	No	LOW
			Seed	Soybean (C) (I) (T)	Yes	Yes	No	LOW
9	Cucurbit Vegetables	Yes	Foliar	Cucumber (T) Pumpkin (C) (T) Watermelon (I)	Yes	Yes	Yes	RISK: Strongest
			Soil	Cucumber (C) (T) Melons (C) (D) (I) (T) Pumpkin (C) (D) (T) Squash (C) (D) (T)	Yes	Yes	Yes	RISK: Moderate
10	Citrus Fruits ⁶	No ⁷	Soil	NA	NA ³	NA	NA	LOW
		Yes	Post-bloom; Soil	Orange (C) Lemon (C)	Yes	Yes	Yes	RISK: Moderate

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data used quantitatively ⁸	Individual Bee (Tier I) Risk		Honey Bee Colony Risk (Tier II)?	Risk Conclusions ^{2,3}
					On Field (Default)	On Field (Refined)		
11	Pome Fruits	Yes	Foliar: post-bloom	Almond (C) Apple (C) Cherry (D) (I) (T) Peach (D) Peach (C) (T) Plum (T)	Yes	Yes	No	LOW
12	Stone Fruits	Yes	Foliar: post-bloom	Almond (C) Apple (C) Cherry (D) (I) (T) Peach (D) Peach (C) (T) Plum (T)	Yes	Yes	No	LOW
13	Berry and Small Fruit	Yes	Foliar: Pre-bloom (Grape, only)	Grape (C)	Yes	Yes	Yes	RISK: Strongest
			Foliar: Post-Bloom	Grape (C)	Yes	Yes	No	LOW
			Soil: Pre-bloom (Grape, only)	Grape (C)	Yes	Yes	No	LOW
			Soil: Post-bloom	Blueberry (I)	Yes	NA	NA	LOW
14	Tree Nuts	Yes	Foliar: Post-bloom	Almond (C) Apple (C) Cherry (D) (I) (T) Peach (D) Peach (C) (T) Plum (T)	Yes	Yes	No	LOW
15	Cereal Grains	No	Foliar (rice-only)	No	NA ³	NA	NA	LOW ⁴

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data used quantitatively ⁸	Individual Bee (Tier I) Risk		Honey Bee Colony Risk (Tier II)?	Risk Conclusions ^{2,3}
					On Field (Default)	On Field (Refined)		
		Yes	Soil (corn-only)	Corn (C)	Yes	Yes	No	LOW
			Seed	Corn (C) (I) (T)	Yes	Yes	No	LOW
20	Oilseed	Yes	Foliar: Cotton-only	Cotton (C)	Yes	Yes	Yes	RISK: Strongest
			Seed	Cotton (C) (T) Canola (T)	Yes	No	No	LOW
23	Tropical and Subtropical Fruit	No	Foliar: post bloom (Figs-only)	Almond (C) Almond (C) Apple (C) Cherry (D) (I) (T) Peach (D) Peach (C) (T) Plum (T)	NA ³	NA	No	LOW
24	Tropical and Subtropical Fruit	Unknown	Foliar: post bloom (Pomegranate-only;)	Almond (C) Apple (C) Cherry (D) (I) (T) Peach (D) Peach (C) (T) Plum (T)	Yes	NA	Yes	LOW
None	Artichoke	No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No		NA	NA	LOW ⁴
	Tobacco	No	Foliar	No	NA ³	NA	No	LOW ⁴
			Soil	No	NA ³	NA	No	LOW ⁴
	Sod	No	Foliar	No	NA ³	NA	NA	LOW ⁴
	Turf/Lawns	Yes ⁹	Foliar	No	Yes	NA	NA	RISK: Moderate
	Ornamentals	Yes	Foliar ¹⁰	Stargazer Lily (T) Mock Orange (T) Lilac (T)	Yes	NA	Yes	RISK: Strongest

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data used quantitatively ⁸	Individual Bee (Tier I) Risk		Honey Bee Colony Risk (Tier II)?	Risk Conclusions ^{2,3}
					On Field (Default)	On Field (Refined)		
			Soil ¹⁰	Hedge Cotoneaster (T) Lilac (T) Sargeant Crabapple (T)	Yes	NA	Yes	RISK: Strongest
	Other outdoor residential uses ¹¹	No	Spray	No	NA ³	NA	NA	LOW ⁴

NA = not assessed.

¹Based on USDA. 2017. Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen.

²Green indicates low risk; red indicates risk.

³If crop is not attractive to bees or is harvested prior to bloom (USDA 2017), RQs are not calculated and risk conclusion is "LOW."

⁴For uses where the crop is grown for food, roots, tubers, bulbs and/or leaves and are harvested prior to bloom (USDA 2017). This limits exposure to bees on field, as the crop is not attractive to bees when not flowering. Exposure may occur on the treated field if crop is grown for seed (*i.e.*, the crop is allowed to flower). Although clothianidin may be applied to crops grown for seed, the spatial footprint for these uses is expected to be limited due to low pounds applied and specific geographic areas where crops are grown for seed.

⁵Honey bee attractive crops with no indication of whether they are harvested prior to bloom (USDA 2017) in the root and tuber vegetable crop group include: sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish.

⁶No national registrations present, only Section 18 registrations in Florida and Texas.

⁷During bloom, mandarin orange trees are tented with nets to prevent bees from pollinating their flowers; in these cases, the crop is considered unattractive to honey bees.

⁸Residue data from other field crops and/or chemicals used for exposure analysis [(C) – clothianidin; (D) – dinotefuran; (T) – thiamethoxam; (I) – imidacloprid].

⁹It is assumed that bee-attractive, blooming weeds (*e.g.*, clover, dandelions) may be present on treated lawns

¹⁰Residue data were pre-bloom. Labels do not have pre-bloom restriction; therefore, no distinction is made between risk calls for pre- and post-bloom applications.

¹¹Crack and crevice treatments, perimeter treatment of buildings, etc.

Table[STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Summary of on-field risk findings for honey bee colonies (*Apis mellifera*) for the registered use patterns of thiamethoxam.

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data used quantitatively ¹²	Individual Bee (Tier I) Risk		Honey Bee Colony Risk? (Tier II)	Risk Conclusions ^{2,3}
					On Field (Default)	On Field (Default)		
1	Root and Tuber Vegetables	Yes ⁵	Foliar	No	Yes	Yes	Yes	RISK: Weakest
			Soil	No	Yes	Yes	Yes	RISK: Weakest
		No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed (carrot, potato, sugar beet only)	No	NA ³	NA	NA	LOW ⁴
3	Bulb Vegetables	No	Seed	No	NA ³	NA	NA	LOW ⁴
4	Leafy Vegetables	No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed	No	NA ³	NA	NA	LOW ⁴
5	Brassica Leafy Vegetables	No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed	No	NA ³	NA	NA	LOW ⁴
6	Legume Vegetables	Yes	Foliar	Soybean (I) (T)	Yes	Yes	No	LOW ⁴
			Seed	Soybean (C) (I) (T)	Yes	Yes	No	LOW ⁴
8	Fruiting Vegetables	Yes ⁶	Foliar	Tomato (D) (T)	Yes	Yes	Yes	RISK: Strongest
			Soil	Tomato (T) (D) Chili (T) Pepper (D)	Yes	Yes	Yes	RISK: Moderate
		No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	Yes	NA	NA	LOW ⁴
9	Cucurbit Vegetables	Yes	Foliar	Cucumber (T) Pumpkin (C) (T) Watermelon (I)	Yes	Yes	Yes	RISK: Strongest
			Soil	Cucumber (C) (T) Melons (C) (D) (I) (T) Pumpkin (C) (D) (T) Squash (C) (D) (T)	Yes	Yes	Yes	RISK: Moderate

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data used quantitatively ¹²	Individual Bee (Tier I) Risk		Honey Bee Colony Risk? (Tier II)	Risk Conclusions ^{2,3}
					On Field (Default)	On Field (Default)		
			Seed	Corn (C) (I) (T) Cotton (C) (T) Canola (T) Soybean (C) (I) (T)	Yes	Yes	No	LOW
10	Citrus Fruits	No ⁷	No	No	NA ³	NA	NA	LOW
		Yes	Foliar: Pre-bloom	Apple (T) Orange (I) (T)	Yes	Yes	Yes	RISK: Strongest
			Foliar: Post-bloom	Almond (C) Apple (C) Cherry (D) (I) (T) Peach (D) Peach (C) (T) Plum (T)	Yes	Yes	No	LOW
			Soil: Pre-bloom	Lemon (C) (T) Orange (C) (T)	Yes	Yes	No	RISK: Strongest
			Soil: Post-bloom	Lemon (C) Orange (C)	Yes	Yes	No	RISK: Weakest
			Foliar: Pre-bloom	Apple (T) Orange (I) (T)	Yes	Yes	Yes	RISK: Strongest
11	Pome Fruits	Yes	Foliar: Post-bloom	Almond (C) Apple (C) Cherry (D) (I) (T) Peach (D) Peach (C) (T) Plum (T)	Yes	Yes	No	LOW
			Foliar: pre-bloom	Apple (T) Orange (I) (T)	Yes	Yes	Yes	RISK: Strongest
12	Stone Fruits	Yes	Foliar: post-bloom	Almond (C) Apple (C) Cherry (D) (I) (T) Peach (D) Peach (C) (T) Plum (T)	Yes	Yes	No	LOW
			Foliar: pre-bloom	Apple (T) Orange (I) (T)	Yes	Yes	Yes	RISK: Strongest

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data used quantitatively ¹²	Individual Bee (Tier I) Risk		Honey Bee Colony Risk? (Tier II)	Risk Conclusions ^{2,3}
					On Field (Default)	On Field (Default)		
13	Berry and Small Fruit	Yes	Foliar: pre-bloom	Blueberry (D) (T) Cranberry (D) (T) Grape (C) Strawberry (T)	Yes	Yes	Yes	RISK: Strongest
			Foliar: post-bloom	Grape (C)	Yes	Yes	Yes	LOW
			Soil: pre-bloom	Strawberry (T) Grape (C)	Yes	Yes	Yes	RISK: Strongest
			Soil: post-bloom	Blueberry (I)	Yes	Yes	Yes	LOW
14	Tree Nuts	Yes	Foliar: Pre-bloom	Apple (T) Orange (I) (T)	Yes	Yes	Yes	RISK: Strongest
			Foliar: Post-bloom	Almond (C) Apple (C) Cherry (D) (I) (T) Peach (D) Peach (C) (T) Plum (T)	Yes	Yes	No	LOW
15	Cereal Grains	No	Foliar (Barley only)	No	NA ³	NA	NA	LOW ⁴
		Yes	Seed	Corn (C) (I) (T)	Yes	No	NA	LOW
18	Forage Fodder, Straw and Hay	Yes	Seed (alfalfa only)	Corn (C) (I) (T) Cotton (C) (T) Canola (T) Soybean (C) (I) (T)	Yes	Yes	No	LOW
19	Herbs and Spices	Yes	Foliar (mint only)	No	Yes	Yes	Yes	RISK: Weakest ⁸
20	Oilseed	Yes	Foliar (cotton only)	Cotton (C) (D) (I) (T)	Yes	Yes	Yes	RISK: Strongest
			Seed	Cotton (C) (T) Canola (T)	Yes	No	No	LOW
23 & 24	Tropical and Subtropical Fruit	Yes	Foliar: Pre-bloom	Apple (T) Orange (I) (T)	Yes	Yes	Yes	RISK: Strongest

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data used quantitatively ¹²	Individual Bee (Tier I) Risk		Honey Bee Colony Risk? (Tier II)	Risk Conclusions ^{2,3}
					On Field (Default)	On Field (Default)		
			Foliar: Post-bloom	Almond (C) Apple (C) Cherry (D) (I) (T) Peach (D) Peach (C) (T) Plum (T)	Yes	Yes	No	LOW
None	Artichoke	No	Foliar	No	NA ³	NA	NA	LOW ⁴
	Tobacco	No	Foliar	No	NA ³	NA	NA	LOW ⁴
	Peanuts	Yes	Seed	Corn (C) (I) (T) Cotton (C) (T) Canola (T) Soybean (C) (I) (T)	Yes	Yes	No	LOW
	Sod	No	Foliar	No	NA ³	NA	NA	LOW ⁴
	Turf/Lawns	Yes ⁹	Foliar	No	Yes	NA	NA	RISK: Moderate ⁹
	Ornamentals	Yes	Foliar ¹⁰	Stargazer Lily (T) Mock Orange (T) Lilac (T)	Yes	Yes	Yes	RISK: Strongest
			Soil ¹⁰	Hedge Cotoneaster (T) Lilac (T) Sargeant Crabapple (T)	Yes	Yes	Yes	RISK: Strongest
	Christmas tree plantation	No	Soil	No	NA ³	NA	NA	LOW ⁴
	Other outdoor residential uses ¹¹	No	Spray	No	NA ³	NA	NA	LOW ⁴

NA = not assessed.

¹Based on USDA. 2017. Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen.

²Green indicates low risk; red indicates risk.

³If crop is not attractive to bees or is harvested prior to bloom, RQs are not calculated and risk conclusion is "LOW."

⁴For uses where the crop is grown for food, roots, tubers, bulbs and/or leaves and are harvested prior to bloom (USDA 2017). This limits exposure to bees on field, as the crop is not attractive to bees when not flowering. Exposure may occur on the treated field if crop is grown for seed (*i.e.*, the crop is allowed to

flower). Although thiamethoxam may be applied to crops grown for seed, the spatial footprint for these uses is expected to be limited due to low pounds applied and specific geographic areas where crops are grown for seed.

⁵Honey bee attractive crops with no indication of whether they are harvested prior to bloom (USDA 2017) in the root and tuber vegetable crop group include: sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish.

⁶Honey bee-attractive crops in the fruiting vegetable crop group include: roselle, okra and chilies and peppers (USDA 2017).

⁷During bloom, mandarin orange trees are tented with nets to prevent bees from pollinating their flowers; in these cases, the crop is considered unattractive to honey bees.

⁸Residue data from other field crops used for exposure analysis (including cucurbits, fruiting vegetables).

⁹It is assumed that bee-attractive, blooming weeds (*e.g.*, clover, dandelions) are present on treated lawns.

¹⁰Residue data were pre-bloom. Labels do not have pre-bloom restriction; therefore, no distinction is made between risk calls for pre- and post-bloom applications.

¹¹Crack and crevice treatment of patios, perimeter treatment of buildings, and barrier treatments of garbage cans.

¹²Residue data from other field crops and/or chemicals used for exposure analysis [(C) – clothianidin; (D) – dinotefuran; (T) – thiamethoxam; (I) – imidacloprid]).

1.3 Risk Conclusions Summary: Bumble bees and other bee species (non-*Apis*)

Comparisons of available Tier I toxicity data for non-*Apis* species, including bumble bees, indicates that honey bees have similar sensitivity to clothianidin and thiamethoxam as the sensitivity exhibited by other bee species to these compounds. An analysis of food consumption rates (of pollen and nectar) for several species of bees suggests that honey bees are similar or protective of other species. Therefore, honey bees represent an appropriate surrogate for assessing individual level risks to other species of bees. Tier I conclusions for honey bees then are therefore also used to represent risks to solitary bees. One notable exception relates to differences in attractiveness of crops. For example, many of the fruiting vegetables are not attractive to honey bees but are attractive other species of bees (*e.g.*, *Bombus sp.*). Therefore, additional crops in the fruiting vegetables group that were considered low risk to honey bees may pose a risk to non-*Apis* bees.

For higher-tiered testing, collectively, potential effects on social non-*Apis* species were reported at the Tier II and III level from exposure to clothianidin at concentrations/doses lower than the registrant-submitted colony feeding studies with honey bees (MRIDs 49836101, 50312501, 50478501 – Clothianidin; 49757201, 50432101– Thiamethoxam), but not in all cases. This suggests that for uses with risk based on Tier II assessments, there are also risk concerns for other social species of bees, such as bumble bees. However, these studies have limitations, were classified as supplemental, and were used qualitatively as no process has been developed for quantifying risks to non-*Apis* species. As such, while there may be potential effects to non-*Apis* species, the ability to reliably determine a no-effect concentration is limited. As the bee risk assessment framework used by the EPA indicates the honey bees are intended to be reasonable surrogates for other bee species, conclusions from the weight of evidence for the honey bee can be used to help inform about potential risks to other non-*Apis* species.

1.4 Environmental Fate and Exposure Summary and Residue Bridging Approach

Exposure of bees through direct contact by foliar applications of clothianidin and thiamethoxam (*i.e.*, interception of spray droplets either on or off the treated field) and oral ingestion (*e.g.*, consumption of residues in pollen and/or nectar) represent the primary routes of exposure considered in this assessment. Potential exposure from crops harvested prior to bloom or those that are not considered attractive to bees (USDA 2017) are also considered in risk conclusions. As previously mentioned, Tier I exposure estimates are generated with EFED's BeeREX model. A comparison of BeeREX estimated environmental concentrations (EECs) to measured residues in pollen and nectar collected from crops treated with clothianidin or thiamethoxam indicates varying levels of confidence in the model's predictive accuracy. For example, modeled values for foliar applications can vary from being on the same order of magnitude up to several orders of magnitude higher than measured residues. To reduce this potential uncertainty, where possible quantification of exposure is refined using measured concentrations of clothianidin and thiamethoxam in pollen and nectar obtained in field studies. At the individual bee level maximum empirical residue values are compared to laboratory toxicity assay endpoints, while at the colony levels residues over time are compared to a semi-field colony no effect concentration. For each chemical, these residue studies were mostly conducted at the maximum labeled application rates generally resulting in pollen concentrations an order of magnitude above nectar concentrations. Measured concentrations of clothianidin and thiamethoxam in pollen and nectar from field residue studies are available across a variety of crop groups.

While refined exposure estimates via empirical residues are available for many crops (*e.g.*, those listed above), there are still gaps in the knowledgebase⁶ for several remaining crops and application types (*e.g.*, foliar spray or soil drench), leading to uncertain exposure potential. There is also uncertainty in the degree to which empirical residues from a single crop may be representative of potential exposures across an entire crop group that may or may not be biologically similar. To fill in these gaps, this assessment uses a residue bridging approach for quantifying dietary neonicotinoid exposure to colonies (Tier II) from use of clothianidin and thiamethoxam. In this approach, measured residue data from four neonicotinoids⁷ in the nitroguanidine-substituted class are pooled by crop group and application type and analyzed for use as surrogate values in bee-relevant matrices where empirical data are not available for a chemical or crop. Where data allowed (primarily for some foliar applications), the Agency employed a Monte Carlo approach to estimate median and upper bound exposure values over time, based on the empirical data and assumptions of single first order (SFO) kinetics.

In addition to contact from spray and ingestion of dietary residues in pollen/nectar, bees may also be exposed to clothianidin and thiamethoxam through other routes, such as ingestion of contaminated surface water, plant guttation fluids, honey dew, contact with/ingestion of soil (for ground-nesting non-*Apis* bees) and leaves (for cavity-nesting non-*Apis* bees). However, the Agency lacks information to understand the relative importance of these other routes of exposure and/or to quantify potential risks from these other routes, and as such, they are not quantitatively assessed. Exposure of bees to clothianidin and thiamethoxam via drift of abraded seed coat dust, is considered a route of concern given that bee kill incidents have been associated with planting of clothianidin or thiamethoxam-treated corn. However, the Agency is working with different stakeholders to identify best management practices and to promote technology-based solutions that reduce this potential route of exposure. To date, the Agency has not developed an approach to quantify this route and as such, this exposure route was not quantitatively considered in this assessment.

1.5 Effects Summary

Clothianidin and thiamethoxam are systemic insecticides in the N-nitroguanidine group of neonicotinoids (IRAC subclass 4A)⁸ along with imidacloprid and dinotefuran. Their mode of action on target insects involves out-competing the neurotransmitter, acetylcholine for available binding sites on the nicotinic acetylcholine receptors (nAChRs). At low concentrations, neonicotinoids cause nervous stimulation. At high concentrations the effect on insects is paralysis and death. Clothianidin and thiamethoxam are xylem and phloem- mobile systemic compounds in plants and are readily taken up by the roots of the plant and translocated throughout the plant via the transpiration stream. As such, they affect insects via ingestion or direct contact of spray droplets as routes of exposure. Target pests include the chewing and sucking pests such as aphids, whiteflies, thrips, leafhoppers, scales, and leaf miners.

Tier I Evaluation

Tier I laboratory toxicity data are available for honey bees and other species of non-*Apis* bees, including bumble bees (*Bombus* sp.) exposed to thiamethoxam and clothianidin. Data considered suitable for

⁶Of empirical residues in plant matrices. This assessment focuses on bee relevant forage matrices (*i.e.*, pollen and nectar).

⁷ Clothianidin, Thiamethoxam, Dinotefuran, and Imidacloprid

⁸ [HYPERLINK "<http://www.irac-online.org/modes-of-action/>"]

deriving acute risk quotients for adult honey bees are available for both chemicals. These data indicate that thiamethoxam and clothianidin are of similar toxicity in both acute and chronic exposure tests. For the chronic endpoints, due to dose spacing and nature of hypothesis-based endpoints (as opposed to regression based) the endpoints are an order of magnitude different; however, examination of the percent effects at the test doses are more similar for both chemicals and support an equal toxicity assumption. Exposure levels of thiamethoxam are expressed as clothianidin equivalents by adjusting for the ratio of the molecular weight of clothianidin to thiamethoxam (*i.e.*, ratio=0.856). **Table 1.3** includes the toxicity endpoints that are considered quantitative and are used to derive RQs.

Tier II Evaluation

Five, Tier II toxicity studies in which honey bee colonies were fed clothianidin and/or thiamethoxam via spiked sucrose (2 per chemical⁹) or spiked pollen (1 for clothianidin) over an extended period of time (referred to as colony feeding studies, or CFSs) were used in this higher-tiered evaluation. Similar effects, including a decline in the number of adult females (workers) and pollen stores followed by a decline in brood (eggs, larvae, and pupae), were observed across the four sucrose-based CFS studies (**Table 1.3**). High variability in some measurements (*e.g.*, thiamethoxam adult workers) resulted in difficulty detecting statistically significant ($p < 0.05$) differences for these parameters; however, trends are generally consistent across studies. Often, the declines in brood were observed weeks after the impacts to workers were observed. This suggests that the impacts on brood were not likely a direct effect, but rather a colony response to a decline in number of workers and/or pollen reserves. Often, the declines in brood were observed weeks after the impacts to workers were observed. It is noted that the initial CFS studies had unsuccessful overwintering components due to poor control survival during overwintering. However, both repeat sucrose-based studies had successful overwintering and increased the Agency's understanding of colony level effect levels. Results from these two studies were generally supportive of the previous two.

For clothianidin, the sucrose based no observed effect concentration (NOAEC) was 19 ng c.e./g and lowest observed effects concentration (LOAEC) was 35.6 ng c.e./g (based on significant impacts to numbers of live adult and brood life stage endpoints, as well as pollen storage, relative to controls) were used in the Tier II analysis. The thiamethoxam Tier II evaluation considers both the clothianidin CFS endpoints and the thiamethoxam-specific endpoints. When evaluating residue data in nectar for thiamethoxam, the (NOAEC) was 43.6 ng c.e./g and the (LOAEC) was 81.7 ng c.e./g. The effect concentrations from the clothianidin CFS are consistent with the effect concentrations from the thiamethoxam CFS. The apparent difference in toxicity is an artifact of the statistical analysis and the magnitude of deviation from controls is similar at comparable concentrations in all 4 sucrose-based studies. The extent to which thiamethoxam is less toxic on a colony basis is not strongly supported. Because these effect concentrations from the clothianidin CFS are generally consistent with the effect concentrations from the thiamethoxam CFS both endpoints are considered in the thiamethoxam risk assessment.

In a pilot CFS study using spiked clothianidin pollen patties, effects on multiple life stages and food storage were observed at the highest treatment rate (1460 ng c.e./g). Effects to a food storage component (uncapped nectar) were also observed at the 372 ng c.e./g treatment rate; however, similar effects were not observed in other food storage components (*e.g.*, pollen stores, capped honey or combined honey & nectar). Therefore, the NOAEC of 372 ng c.e./g is based on the effects to apical endpoints (adults, eggs, pupae) observed in the 1460 ng c.e./g treatment group.

⁹ There first two studies MRIDs 49836101 and 49757201 respectively for thiamethoxam and clothianidin did not achieve overwintering and were repeated by the registrant.

At the Tier II level, this risk assessment uses a total dietary approach to consider exposures through pollen and nectar. Exposures to residues in pollen are evaluated by converting them to nectar equivalents, using pollen residues divided by a factor of 20. This factor was arrived at using multiple lines of evidence including their differential relative consumptions at the colony level (based on BeeREX food consumption rates), the empirical consumption rates observed in the control colonies in the clothianidin-spiked sucrose and spiked pollen CFS studies and open literature data on colony consumption requirements. The effects observed in the clothianidin-spiked sucrose and spiked pollen studies also suggested an approximately 20x difference between the nectar and pollen based exposures in that effects observed at the clothianidin-spiked pollen LOAEC of 1460 ng c.e./g were similar in nature and magnitude to the effects observed at the clothianidin spiked sucrose treatment rate of 75 ng c.e./g. Given that differences in colony-level effects between clothianidin and thiamethoxam, sucrose-based CFS studies were not conclusively supported; therefore, the evaluation of colonies exposed to pollen with thiamethoxam contaminated residues also uses the 20x factor for the derivation of nectar equivalents.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Acute and chronic toxicity endpoints used for assessing risk to bees from exposure to clothianidin and thiamethoxam.

Study Type	Measurement Endpoint	Clothianidin	Thiamethoxam	MRID (clothianidin /thiamethoxam)
Tier I (units: µg c.e./bee/day)				
Adult Acute Contact Toxicity	96-hr LD ₅₀	0.0275	0.021	49950102 44714927
Adult Acute Oral Toxicity	48-hr LD ₅₀	0.0037	0.0038	45422426 49005702
Adult Chronic Oral Toxicity	10-day NOAEL/LOAEL	0.00036/0.00072 (12% mortality)	0.0025/0.0049 (70% mortality)	48414901 50084901
Larval Acute (single dose)	LD ₅₀	NA	>0.03	NA 50096607
Larval Chronic (repeat dose)	21-day NOAEC/LOAEC	NA	0.0037/0.0066 (adult emergence)	NA 50096607
Tier II (units: ng c.e./g)				
Colony Feeding Study (spiked sucrose)	Colony NOAEC/LOAEC	19/35.6 (decrease in number of adults, brood, and pollen cells)	43.6/81.7 (decrease in numbers of brood)	49836101 50432101

c.e. = clothianidin equivalent

1.6 Major Assumptions and Uncertainties

There are several assumptions and uncertainties associated with both the effects and exposure assessments for clothianidin and thiamethoxam. While these assumptions and uncertainties are described in further detail throughout this assessment, a list of the major assumptions and uncertainties is provided below:

- Direct contact and consumption of pollen and nectar are assumed to be the dominant routes of exposure for bees. Potential exposure via abraded seed coat dust is being addressed through separate ongoing development of best management practices.

- It is assumed that pollen and nectar are equally potent routes of exposure when assessing the risk to individual bees. At the colony level, an evaluation of toxicity data from separate nectar (sucrose) and pollen exposures indicates that the matrix does not influence toxicity.
- Honey bees serve as a surrogate for other bees. In this approach, it is assumed that data on individual honey bees as well as colony-level data can provide relevant information on the potential effects of a pesticide on solitary bees and social bees
- Off-field estimates of risk are based on screening-level exposure estimates which cannot be refined with available residue data and are assumed to be to bee friendly crops at the time of bloom. Therefore, potential off-field risks may be overestimated.
- Interpretation of Tier 2 risks based on the 6-week, sucrose colony feeding study assumes that bees forage on the treated crop nearly 100% of the time to represent the nectar needs of the colony. In the field, bees may forage for significantly shorter periods of time particularly for crops such as cherries and blueberries that have a 2-3 weeks blooming duration. Bees may also forage on alternative (untreated) plants. Conversely, bees associated with migratory colonies used for pollination services may feed on treated crops for similar or possibly longer periods of time over the course of a growing season.

2 Problem Formulation

Problem formulation serves as the first step of a risk assessment and it provides the foundation for the entire ecological risk assessment. In addition to identifying the risk assessment scope and objectives, the problem formulation includes three major components: (1) assessment and measurement endpoints that reflect management goals and the ecosystem they represent; (2) conceptual models that describe key relationships between a stressor (*i.e.*, pesticide) and assessment endpoint; and, (3) an analysis plan that summarizes the key sources of data and methods to be used in the risk assessment (USEPA 1998).

2.1 Registration Review Background

As articulated by the Agency's Registration Review schedule, the nitroguanidine-substituted neonicotinoid insecticides (imidacloprid, clothianidin, thiamethoxam, and dinotefuran) are currently undergoing Registration Review. This document is the final revised Registration Review pollinator risk assessment for thiamethoxam and clothianidin, and incorporates new data and consideration of public comments received since the publication of the preliminary pollinator risk assessment in 2017. The clothianidin Registration Review docket can be accessed at [HYPERLINK "<http://www.regulations.gov/>" \h] at docket number EPA-HQ-OPP-2011-0865, and thiamethoxam is available at EPA-HQ-OPP-2011-0581. Additional details, including previously published documents regarding the schedules and dockets for clothianidin, thiamethoxam, and the other neonicotinoids can be accessed online at: [HYPERLINK "<http://www.epa.gov/pollinator-protection/schedule-review-neonicotinoid-pesticides>" \h] [HYPERLINK "<http://www.epa.gov/pollinator-protection/schedule-review-neonicotinoid-pesticides>" \h].

2.2 Nature and Scope of Assessment

Unlike most of the ecological risk assessments written in support of the Registration Review of pesticides which focus on multiple aquatic and terrestrial non-target organisms, this assessment focuses solely on the potential risks to bees from registered uses of clothianidin and thiamethoxam.

Typically, EFED's assessments consider the risks associated with a single active ingredient and potentially any degradates of concern. This assessment considers both clothianidin and thiamethoxam active ingredients in the same document for the following reasons:

- 1) Available data suggest that thiamethoxam is metabolized by plants to form clothianidin (see **Section 3.3** for details);
- 2) In environmental fate studies of thiamethoxam, clothianidin forms as a minor degradate in aerobic soil metabolism studies (2.0-4.7%) and a major degradate in a terrestrial field dissipation study (13.2%). Therefore, clothianidin available in the environment may be from pesticide applications of clothianidin products, or as a result of thiamethoxam applications and the subsequent degradation of thiamethoxam to clothianidin.
- 3) The toxicity of clothianidin and thiamethoxam to bees is similar (**See Section 4**)¹⁰.

¹⁰ This assessment uses this assumption at the tier 1 level of analysis (individual bees). The tier 2 analysis considers both endpoints as the thiamethoxam endpoint is about 2X less sensitive than clothianidin at the honeybee colony level; however, percent effects at similar dose levels are not supportive of toxicity difference.

- 4) Although there are no end-use products co-formulated with both clothianidin and thiamethoxam, each chemical has formulated products registered for use on the same crops.

Exposures of thiamethoxam are expressed as clothianidin equivalents by adjusting for the ratio of the molecular weight of clothianidin to thiamethoxam (*i.e.*, 0.856). While the Tier II analysis considered toxicity weighting as the thiamethoxam endpoint is about 2X less sensitive than clothianidin based on the evaluated studies, an analysis of the data suggested this was an artifact of the dose spacing as percent effects at similar doses were not sufficiently different to support a toxicity weighting factor. For residue data where both thiamethoxam and clothianidin residues are reported on a weight basis (*i.e.*, ng/g) within a study, thiamethoxam residues are first adjusted to clothianidin equivalents (“c.e.”), and are then added to measured concentrations of clothianidin in the same sample to derive a total residue concentration. Residues of thiamethoxam and clothianidin were not combined across different residue studies or use profiles. For consistency across the two chemicals in this assessment, clothianidin residues are also reported as “c.e.”, even though they were not “adjusted”.

The decision to focus on clothianidin’s and thiamethoxam’s potential risks to bees reflects the Agency’s desire to identify potential risks and possible mitigation measures earlier in the Registration Review process. It also reflects the large volume of information and research related to environmental exposure and effects of clothianidin and thiamethoxam to bees. Assessments involving thiamethoxam and clothianidin considering the ecological risks to other taxa were published in 2017.

Several other aspects related to the scope of this Final Pollinator Risk Assessment (FPRA) are important to note. First, this assessment includes a quantitative estimate of risk (*i.e.*, derivation of risk quotients) for the honey bee, *Apis mellifera*. Other non-*Apis* bees are also considered in this assessment including social non-*Apis* bees (bumble bees; *Bombus* spp.) and solitary non-*Apis* bees (*e.g.*, *Osmia* spp), but potential risks to these species are evaluated qualitatively (*i.e.*, without derivation of risk quotients) due to limitations in available data and risk assessment methods for these species. This approach is consistent with the Agency’s Guidance for Assessing Pesticide Risks to Bees (USEPA/PMRA/CDPR 2014) which recognizes that methods and data for assessing pesticide effects (and exposure) to bumble bees and solitary bees are still evolving.

Second, unlike the preliminary risk assessment (USEPA 2016) this revised assessment considers all registered agricultural and non-agricultural uses of clothianidin and thiamethoxam.

Third, the effects data (*i.e.*, measurement endpoints) considered in this assessment are consistent with the Agency’s protection goals and associated assessment endpoints previously identified for bees (USEPA/PMRA/CDPR 2014). As described further in **Section 2.7**, the assessment and measurement endpoints used to support these protection goals are those that closely relate to survival, growth and reproduction of individual bees and overall colony strength and survival (for social bees). A large body of literature has been generated on effects of clothianidin and thiamethoxam on bees at lower levels of biological organization (*e.g.*, molecular, organ-level effects) in addition to numerous sub-lethal endpoints relating to behavioral, physiological aspects of individual bees. While such data are useful for consideration as additional lines of evidence in risk assessment and understanding the mechanisms of

toxicological effects, they were formally evaluated in this assessment only when they could be quantitatively linked to Agency assessment endpoints described in **Section 2.7**. This assessment also includes a review of additional open literature related to effects of thiamethoxam and clothianidin on bees at lower levels of biological organization evaluated since the preliminary risk assessment.

2.3 Pesticide Type, Class, and Mode of Action

Clothianidin and thiamethoxam are insecticides in the N-nitroguanidine subclass of neonicotinoids (IRAC subclass 4A; IRAC 2015) along with imidacloprid and dinotefuran. Their mode of action on target insects involves out-competing the neurotransmitter, acetylcholine for available binding sites on the nAChRs (Zhang *et al.* 2008). At low concentrations, neonicotinoids cause nervous stimulation and at high concentrations, insect paralysis and death will occur (Tomizawa and Casida 2005).

Clothianidin and thiamethoxam are xylem- (acropetal systemicity) and phloem-mobile (basipetal) systemic compounds that are readily taken up by the roots of the plant and translocated throughout the plant via the transpiration stream. As such, they kill insects via ingestion of residues in plant materials or via direct contact. Target pests include the chewing and sucking pests such as aphids, whiteflies, thrips, leafhoppers, scales, and leaf miners.

2.4 Overview of Uses

Clothianidin and thiamethoxam may be applied to crops via a variety of methods including aerial and ground foliar sprays, soil treatment (*e.g.*, drench), chemigation (*e.g.*, soil incorporation or foliar), and as a seed treatment. Clothianidin and thiamethoxam are used on a wide array of agricultural crops, including (but not limited to): root and tuber vegetables, leafy vegetables, brassica, cucurbits, fruiting vegetables, cereal grains, citrus fruit, pome fruit, stone fruit, berries, tree nuts, beans and other legumes, herbs, oilseed crops (*e.g.*, canola, cotton), and tobacco. There are currently 42 registered Section 3 end-use products for clothianidin and 78 end-use products for thiamethoxam.

When considering the same uses, single maximum application rates allowed for clothianidin for foliar sprays are generally higher than those allowed for thiamethoxam (**Table 2-1**). Maximum single application rates allowed for clothianidin are 0.1 or 0.2 lb a.i./A (pounds of active ingredient per acre) for most crops; whereas, maximum single application rates for thiamethoxam are 0.047, 0.063 or 0.086 lb a.i./A (expressed as clothianidin equivalents¹¹: 0.040, 0.054 or 0.074 lb c.e./A, respectively). Clothianidin and thiamethoxam are also registered for use as soil and for seed treatments on several crops (**Tables 2-2** and **2-3**). Where the table indicates “all registered uses” it includes the set or subset of actual registered crops within a crop group. It does not mean that all crops are registered for either clothianidin or thiamethoxam within that crop group.

The refined exposure analysis for seed treatment utilizes treatment rates expressed in mg a.i./seed. Rates expressed in **Table 2-3** are in either lb a.i./seed or lb a.i./lb-seed. **Table 2-4** includes the rates expressed as mg a.i./seed. This was calculated by either converting lb a.i./seed to mg a.i./seed using standard unit

¹¹ As discussed in the analysis plan (section 2.8), application rates, concentrations, and toxicity values for
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conversions. If rates were expressed as lb a.i./lb-seed, the mass of ai was converted to mg and the value was multiplied by the weight of a seed.

Additionally, thiamethoxam is registered as a soil treatment to non-bearing fruit and nut trees. These applications are not agricultural uses, but rather ornamental uses. There are also a wide variety of non-agricultural uses of clothianidin and thiamethoxam (**Table 2-5**), some examples of which include forestry, turf, and applications to ornamentals. This assessment updates the preliminary assessment to address these use patterns.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Maximum application rates for foliar applications of clothianidin and thiamethoxam.

Use	Clothianidin				Thiamethoxam			
	Single App rate (lb c.e./A)	# of Apps	App. Interval (d)	Method	Single App rate (lb a.i./A; value in parentheses is lb c.e./A)	# of Apps	App. Interval (d)	Method
Crop Group 1 – Root and Tuber Vegetables								
Root and tuber vegetables, Crop Group 1 – Except listed below	0.05	4	7	c, g	0.05 (0.043)	2	7	a, g
Crop Subgroup 1A. Root Vegetables subgroup: Sugar beet	Not Registered				0.063 (0.053)	2	7	a, g
Crop Subgroup 1B. Root vegetables (except sugar beet), - Except listed below	NA	NA	NA	NA	0.063 (0.053)	2	7	a, g
Radish	Not Registered				0.063 (0.053)	1	NA	a, g
Crop Subgroup 1C. Tuberous and corm vegetables subgroup: Potato	0.05	4	7	a, c, g	0.05 (0.043)	2	7	a, g
Crop Subgroup 1D. Tuberous and corm vegetables subgroup: Turmeric	0.05	4	7	c, g	NA	NA	NA	NA
Crop Group 4 – Leafy Vegetables (Except brassica Vegetables)								
All registered uses	0.1	2	10	c, g	0.088 (0.075)	2	7	a, g
Crop Group 5 – Brassica (Cole) Leafy Vegetables								
All registered uses	0.1	2	7	g	0.088 (0.075)	2	7	a, g
Crop Group 6 - Legume Vegetables (Succulent or Dried)								
Soybeans	0.1	2	7	a, c, g	0.063 (0.053)	2	7	a, g
Crop Group 8 – Fruiting Vegetables (Except Cucurbits)								
All registered uses	Not Registered				0.088 (0.075)	2	5	a, g
Crop Group 9 – Cucurbit Vegetables								
All registered uses	0.1	2	7	c, g	0.088 (0.075)	2	5	a, g
Crop Group 10 – Citrus								
All registered uses	Not Registered				0.088 (0.075)	2	7	a, g
Crop Group 11 – Pome Fruits								

All registered uses – Except listed below	0.2	1	--	g, post- bloom only	0.086 (0.074)	3	10	g
Crop Group 12 – Stone Fruits								
All registered uses	0.2	1	--	g, post- bloom	0.086 (0.074)	2	7	g
Crop Group 13-07 – Berry and Small Fruit								
Subgroup A: Caneberries	Not Registered				0.047 (0.040)	2	7	a, g
Subgroup B: Bushberries	0.067	3	7	c,g; post- bloom only	0.063 (0.053)	2	7	a, g
Grapes	0.1	2	14	c, g	0.056 (0.048)	2	14	a, g
Subgroup E: Small Fruit, climbing vine (except grape)	Not Registered				0.055 (0.047)	2	14	a, g
Strawberries	Not Registered				0.063 (0.053)	3	10	g
Subgroup H: Low growing berries (except strawberry)	0.067	3	7	c,g, post- bloom only	0.063 (0.053)	2	10	g
Crop Group 14 – Tree nuts								
All registered uses	0.1	2	10	g, post- bloom only	0.063 (0.053)	2	7	a, g
Crop Group 15 – Cereal Grains								
Barley	Not Registered				0.063 (0.053)	2	7	a, g
Rice	0.075	1	--	a, g	Not Registered			
Crop Group 19 – Herbs and Spices								
Mint	Not Registered				0.063 (0.053)	3	14	a, g
Crop Group 20 – Oilseed								
Cotton	0.102	2	7	a, c, g	0.063 (0.053)	2	5	a, g
Crop Group 23 – Tropical and Subtropical Fruit, Edible Peel Group								
All registered uses – Except listed below	Not registered except for fig				0.063 (0.053)	3	7	a, g
Fig	0.1	2	14	c, g				
Crop Group 24 – Tropical and Subtropical Fruit, Inedible Peel Group								
All registered uses – Except listed below	Not registered except for pomegranate				0.063 (0.053)	3	7	a, g
Pomegranate	0.1	2	14	g				
Other Crops								
Artichoke	0.05	4	7	c, g	0.047	2	7	a, g
Tobacco	0.066	3	7	c, g	0.050	2	3	a, g

				(0.043)			
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NS = Not Specified; NA = not applicable; g= ground; a= aerial; c=chemigation

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Maximum application rates for soil applications of clothianidin and thiamethoxam

Use	Clothianidin			Thiamethoxam		
	Single app rate (lb c.e./A	# of apps	App. interval (d)	Single App rate (lb a.i./A; value in parentheses is lb c.e./A)	# of apps	App. interval (d)
Crop Group 1 – Root and Tuber Vegetables						
All registered uses – Except listed below	0.2	1	--	0.18 (0.16)	1	--
Radish	Not Registered			0.1 (0.08)	1	--
Crop subgroup 1-C. Tuberous and corm vegetables				0.13 (0.1)	1	--
Crop Group 4 - Leafy Vegetables (Except Brassica Vegetables)						
All registered uses	0.2	1	--	0.17 (0.15)	1	--
Crop Subgroup 5-B - Brassica Leafy Greens Subgroup						
All registered uses	0.2	1	--	0.17 (0.15)	1	--
Crop Subgroup 8-10 – Fruiting Vegetables						
All registered uses	Not Registered			0.17 (0.15)	1	--
Crop Group 9 - Cucurbit Vegetables						
All registered uses	0.2	1	NA	0.17 (0.15)	1	--
Crop Group 10 – Citrus						
Citrus (FL)	0.2 ²	2	42-112	0.17 (0.15)	1	--
Crop Group 11 - Pome Fruits						
All registered uses	0.2	1	--	Not registered		
Crop Group 12- Stone Fruit						
All registered uses	0.1	2	10	Not registered		
Crop Group 13-07 – Berry and Small Fruit						
Subgroup B: Bushberries	0.22	1	--	1	--	Not regist ered
Subgroup G:G Low growing berries (except strawberry)	0.2	1	--	0.19 (0.16)	1	--
Grapes	0.2	1	--	0.27 (0.23)	1	--
Strawberries	Not Registered			0.16	1	--
Subgroup: H: low growing berries (except strawberries)	0.2	1	--	Not Registered		

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Use	Clothianidin			Thiamethoxam		
	Single app rate (lb c.e./A	# of apps	App. interval (d)	Single App rate (lb a.i./A; value in parentheses is lb c.e./A)	# of apps	App. interval (d)
Crop Group 15 – Cereal Grains						
Corn ³	0.2	1	NA	Not Registered		
Crop Group 24 – Tropical and Subtropical Fruit, Inedible Peel Group						
Pomegranate	0.1	2	14	Not Registered		
Other Crops						
Artichoke	0.2	1	7	Not Registered		
Tobacco	0.1	2	NS			

NS = not specified

¹ This rate is the result of a label conversion of a rate expressed in terms of lbs per 1000 sq. ft. which was scaled up to a per acre basis. ² For clothianidin, this is a section 18 registration (emergency use).

³ Experimental Use Permit (EUP) for in-furrow soil application for clothianidin to corn

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Seed treatment uses and corresponding application rates registered for clothianidin and thiamethoxam.

Use	Clothianidin		Thiamethoxam	
	lb a.i./seed	lb a.i./lb seed	lb a.i./seed	lb a.i./lb seed
Crop Group 1 – Root and Tuber Vegetables				
Carrot	1.4E-07	NA	1.1E-07	NA
Potato	NA	9.98E-05	NA	6.2E-05
Sugar Beet	1.37E-06	NA	1.6E-06	NA
Turmeric	NA	9.98E-05	Not Registered	
Crop Group 3 – Bulb Vegetables				
Onion	4E-07	NA	4.4E-07	NA
Onion (scallions and leeks)	4.6E-07	NA		
Onion (spring)	2.3E-07	NA		
Crop Group 4 – Leafy Vegetables (Except brassica Vegetables)				
Leafy vegetables (Except Brassica), Crop Group 4	NA	NA	2.7E-06	NA
Amaranth, Chinese	NA	4.42E-02	2.7E-06	NA
Lettuce	NA	NA	1.3E-07	NA
Spinach	NA	NA	2.7E-07	NA
Corn salad	NA	1.9E-02	2.7E-06	NA
Parsley	NA	3.25E-02	NA	NA
Chervil	NA	0.018	NA	NA
Sorrel (dock)	NA	0.036	NA	NA
Crop Group 5 – Brassica (Cole) Leafy Vegetables				
Brassica leafy vegetables, Crop Group 5	2.64E-06	NA	2.2E-07	NA
Crop Group 6- Legume vegetables				
Legume vegetables, Crop Group 6	NA	NA	NA	5.0E-04
Beans	NA	NA	NA	5.0E-04
Soybeans	2.9E-07	5.02E-04	NA	7.5E-04
Lentils	NA	NA	NA	5.0E-04
Peas	NA	NA	NA	2.5E-04

Use	Clothianidin		Thiamethoxam	
	lb a.i./seed	lb a.i./lb seed	lb a.i./seed	lb a.i./lb seed
Crop Group 9 - Cucurbit vegetables				
Cucurbit vegetables, Crop Group 9	NA	NA	1.7E-06	NA
Crop Group 15 – Cereal Grains				
Cereal grains	NA	7.02E-04	NA	5.2E-04
Barley	NA	7.08E-04	NA	5.2E-04
Buckwheat	NA	7.03E-04	NA	5.2E-04
Corn (unspecified)	1.13E-06	NA	2.8E-06	NA
Corn (field)	2.79E-06	NA	1.3E-06	9.9E-04
Corn (pop)	2.79E-06	NA	1.3E-06	2.2E-03
Corn (sweet)	1.12E-06	NA	1.3E-06	1.8E-03
Corn (sweet, ID only)	2.79E-06	NA	NA	NA
Millet	NA	7.08E-04	NA	5.2E-04
Oat	NA	7.08E-04	NA	5.2E-04
Rice	NA	7.5E-04	7.0E-08	NA
Rye	NA	7.08E-04	NA	5.2E-04
Sorghum	NA	2.53E-03	NA	3.0E-03
Teosinte	NA	7.03E-04	NA	5.2E-04
Triticale	NA	7.08E-04	NA	5.2E-04
Wheat	NA	7.08E-04	NA	5.2E-04
Crop Group 20 - Oilseed				
Entire Group – Except listed below	NA	NA	NA	4.0E-03
Canola	NA	4.04E-03	NA	4.0E-03
Cotton	7.78E-07	NA	8.3E-07	NA
Sunflower	NA	NA	5.5E-07	NA
Crop Group 18 – Non-grass Animal Feeds (Forage Fodder, Straw and Hay)				
Alfalfa	Not Registered		1.1E-06	NA
Other Crops				
Peanuts	Not Registered		6.4E-07	4.5E-04

NA = not applicable

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Application rates for seed treatments expressed as mg c.e./seed.

Crop	Seed weight (mg/seed) ^{1,2}	Clothianidin	Thiamethoxam
Alfalfa	NA++	Not registered	0.43
Amaranth, Chinese	10.62 (spinach)	0.47	1.05
Barley	46.86	0.033	0.02
Beans	347.78	NA	0.15
Brassica leafy vegetables (Crop Group 5)	NA++	1.20	0.09
Buckwheat	28.8*	0.021	0.013
Canola	4.43	0.018	0.015
Carrot	NA++	0.06	0.04
Cereal grains	46.86 (barley)	0.033	0.021
Chervil	2.04 (parsley)	0.037	NA+
Corn (field)	NA++	1.27	0.50
Corn (pop)	NA++	1.27	0.50

Crop	Seed weight (mg/seed) ^{1,2}	Clothianidin	Thiamethoxam
Corn (sweet)	NA++	0.51	0.50
Corn (sweet, ID only)	NA++	1.27	NA+
Corn (unspecified)	NA++	0.51	1.09
Corn salad	10.65 (spinach)	0.20	1.05
Cotton	NA++	0.35	0.32
Cucurbit vegetables, Crop Group 9	30.16 (cucumber)	NA+	0.66
Leafy vegetables (Except Brassica), Crop Group 4	1.01 (lettuce)	NA+	1.05
Legume vegetables, Crop Group 6	501.15 (lima bean)	0.25	0.21
Lentils	270.56	NA+	0.12
Lettuce	1.01	NA+	0.05
Millet	5.53+	0.0039	0.0025
Oat	31.28**	0.022	0.014
Oilseed (except canola, cotton, sunflower)	4.43 (oilseed rape)	NA+	0.017
Onion	NA++	0.18	0.17
Onion (scallions and leeks)	NA++	0.21	0.17
Onion (spring)	NA++	0.10	0.17
Parsley	2.03	0.066	NA+
Peanuts	NA++	Not registered	0.25
Peas	218.48	NA	0.047
Potato	56818.18	5.7	3.0
Rice	24+++	0.018	0.03
Rye	31.35***	0.018	0.014
Sorghum	25.25	0.064	0.065
Sorrel (dock)	10.65 (spinach)	0.38	NA+
Soybeans	146	0.13	0.16
Spinach	10.65	NA	0.10
Sugar Beet	NA++	0.62	0.62
Sunflower	NA++	NA	0.21
Teosinte	144.3 (corn)	0.036	0.064
Triticale	31.35 (wheat)	0.022	0.014
Turmeric	56818.18 (potato)	5.7	Not registered
Wheat	31.35	0.022	0.014

NA+ not applicable because different crop or crops in group are registered.

NA++ not applicable because rate already expressed as mass c.e. per seed (**Table 2.3**).

¹From USEPA 2011.

²Surrogate crop listed in parentheses.

*<https://www.hort.purdue.edu/newcrop/afcm/buckwheat.html>

**<https://crops.extension.iastate.edu/cropnews/2016/03/fine-tune-oat-seeding-rate-spring>

***https://www.pennington.com/-/media/files/pennington-na/us/tips_guides/foragecropweightguide.pdf

+https://www.pennington.com/-/media/files/pennington-na/us/tips_guides/foragecropweightguide.pdf

+++ <http://www.deltafarmpress.com/seed-pound-and-average-number-seed-square-foot-rice-varieties>

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Non-agricultural uses and corresponding application rates registered for clothianidin and thiamethoxam.

Use	Clothianidin			Thiamethoxam		
	Single app rate (lb a.i./A)	# of apps	App. interval (d)	Single App Rate (lbs a.i./A) in c.e.	# of apps	App. interval (d)
Turf/Lawns						
Commercial/industrial lawns, golf course turf, ornamental grasses, ornamental lawns and turf, ornamental sod farm (turf), recreation area lawns, residential lawns	0.4	1	N/A	0.266 (0.23)	Not Stated	Not Stated
Ornamentals						
Ornamental ground cover, Christmas tree plantations, Ornamental and/or shade trees, ornamental herbaceous plants, ornamental nonflowering plants, ornamental woody shrubs and vines, greenhouse use	0.4	1	N/A	0.266 (0.23)	Not Stated	7
Other ¹						
Airports/landing fields, animal housing premises (indoor/outdoor), commercial/institutional industrial premises/equipment, commercial storages/warehouses/premises, commercial transportation facilities, household/domestic dwellings, poultry feedlots, ships and boats, wood pressure treatment to forest products, wood protection treatment to buildings/products, vehicles, eating establishments non-food areas, hospitals/medical institutions, pet living quarters, animal kennels, bedding/matresses	1.5	1	N/A	0.266 (0.23)	Not Stated	Not Stated

¹"Other" applications included indoor and outdoor uses that were either baits, spot treatments, void treatments, crack or crevice treatments, perimeter treatments, or wood protection treatment by pressure. Wood protection products are not evaluated in EFED's registration review ecological risk assessment; these antimicrobial uses will be evaluated by the Antimicrobial Division.

According to the usage report provided by the Biological and Economic Analysis Division (BEAD) (thiamethoxam Screening Level Usage Analysis (SLUA) dated 2/10/16), the majority (approximately 80%) of thiamethoxam used on agricultural crops is applied to soybeans (300,000 lbs/year on seeds), corn (300,000 lbs/year on seeds) and cotton (160,000 lbs/year on seeds and plants). The majority of clothianidin (1,400,000 lbs/year) is applied to corn (clothianidin SLUA dated 1/20/16) via seed treatment. For corn, an estimated annual average of 45% of the total crop planted in the US is treated with clothianidin, and 25% is treated with thiamethoxam (maximum of 65% for clothianidin and 45% for thiamethoxam in any given year). Current thiamethoxam and clothianidin end-use product labels restrict use of these chemicals on corn to seed treatment only (except for an experimental use permit for in-furrow soil application for clothianidin). Summaries of the estimated annual usage of clothianidin and thiamethoxam as a seed treatment and foliar/soil treatments are in **Tables 2-6** and **2-7**.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Estimated annual usage of clothianidin and thiamethoxam applied via seed treatment (source: SLUAs) – Reporting Time 2005-2014

Crop	Clothianidin			Thiamethoxam		
	Lbs a.i. applied per year	PCT (annual average)	PCT (annual max)	Lbs a.i. applied per year	PCT (annual average)	PCT (annual max)
Corn	1,400,000	45	65	300,000	25	45
Cotton	9,000	<2.5	<2.5	100,000	30	45
Potatoes	NA	NA	NA	20,000	15	20
Sorghum	5,000	5	15	20,000	20	25
Soybeans	30,000	<2.5	<2.5	300,000	15	25
Sugar beets	10,000	40	55	2,000	5	10
Wheat	4,000	<2.5	<2.5	50,000	5	15
Total	1,458,000	NA	NA	792,000	NA	NA

NA = not applicable

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Estimated annual usage of clothianidin and thiamethoxam applied via foliar or soil applications (source: SLUAs) – Reporting Time 2005-2014.

Crop	Clothianidin			Thiamethoxam		
	Lbs a.i. applied per year	PCT (annual average)	PCT (annual max)	Lbs a.i. applied per year	PCT (annual average)	PCT (annual max)
Alfalfa	NA	NA	NA	<500	<1	<2.5
Almonds	1,000	<2.5	<2.5	NA	NA	NA
Apples	1,000	<2.5	5	2,000	5	20
Artichokes	NA	NA	NA	<500	30	40
Beans, green	NA	NA	NA	<500	<2.5	<2.5
Blueberries	NA	NA	NA	<500	<2.5	<2.5
Broccoli	1,000	5	20	1,000	10	20
Brussels sprouts	<500	<2.5	<2.5	<500	5	15
Cabbage	<500	<2.5	<2.5	<500	5	20
Cantaloupes	<500	<2.5	5	NA	NA	NA
Caneberries	NA	NA	NA	<500	15	25
Cantaloupes	NA	NA	NA	1,000	5	25
Carrots	NA	NA	NA	<500	5	10
Cauliflower	1,000	10	15	<500	5	20
Celery	<500	<1	<2.5	1,000	20	50

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Crop	Clothianidin			Thiamethoxam		
	Lbs a.i. applied per year	PCT (annual average)	PCT (annual max)	Lbs a.i. applied per year	PCT (annual average)	PCT (annual max)
Cherries	NA	NA	NA	1,000	10	25
Chicory	NA	NA	NA	<500	5	10
Cotton	10,000	<2.5	<2.5	60,000	10	15
Cucumbers	<500	<1	<2.5	<500	5	10
Figs	<500	10	15	NA	NA	NA
Dry Beans/Peas	NA	NA	NA	<500	<1	<2.5
Grapefruit	NA	NA	NA	2,000	25	65
Grapes	2,000	<2.5	5	1,000	<2.5	5
Lemons	NA	NA	NA	<500	5	10
Lettuce	<500	<2.5	<2.5	2,000	10	35
Oranges	<500	<1	<2.5	10,000	15	25
Peaches	1,000	5	10	1,000	5	15
Pears	1,000	5	15	1,000	20	35
Pecans	1,000	<2.5	5	<500	<2.5	5
Peppers	<500	<2.5	<2.5	1,000	15	35
Pistachios	NA	NA	NA	<500	<1	<2.5
Plums/Prunes	<500	<1	<2.5	<500	<2.5	<2.5
Pomegranates	<500	<2.5	<2.5	NA	NA	NA
Potatoes	5,000	5	10	20,000	15	30
Pumpkins	<500	<2.5	<2.5	<500	<2.5	10
Soybeans	NA	NA	NA	10,000	<1	<2.5
Spinach	<500	<2.5	<2.5	<500	5	10
Squash	<500	<2.5	<2.5	<500	5	10
Strawberries	NA	NA	NA	1,000	20	40
Tangerines	NA	NA	NA	<500	5	10
Tobacco	<500	<1	<2.5	<500	<2.5	5
Tomatoes	1,000	5	15	6000	10	20
Walnuts	<500	<2.5	<2.5	NA	NA	NA
Watermelons	<500	<2.5	<2.5	<500	5	10
Wheat	NA	NA	NA	<500	<1	<2.5
Total	25,000- 35,500	NA	NA	121,000- 132,500	NA	NA

In this risk assessment, conclusions are made by considering the exposures of bees at the field level. In order to put field level risks into a larger spatial context, pesticide usage data provided by BEAD (in the SLUA) can be applied to acres of crops grown. The SLUA provides information on the average annual percent of crop area treated (PCT) based on 2004-2013 as well as the maximum PCT from any of the years. The sources for the SLUA include the USDA's National Agricultural Statistics Service (NASS, reporting data from 2004 – 2013), private pesticide market research (reporting data from 2004 – 2013), and the CDPR Pesticide Use Reporting (PUR) data (reporting from 2004 – 2012). The average annual pounds of pesticide applied for each crop originates from the states that were surveyed and not the entirety of the United States. It is also noted that usage information for a given crop is available from states that produce 80% or more of that crop in most cases. Lack of reported usage for a given crop does not necessarily indicate zero usage. Although some uses for seed treatment applications are delineated, the SLUA does not distinguish between foliar and soil applications if a given crop is registered for both application methods.

To estimate the annual acres treated, PCT is multiplied by the acres grown per year of each crop. This is obtained from USDA 2017. **Table 2-8** depicts the estimated acres by crop that receive clothianidin or thiamethoxam applications via seed treatment. The majority of acres treated for both crops are represented by corn. When considering all acres treated in the US, 99% of acres treated with clothianidin and 97% of all acres treated with thiamethoxam are via seed treatment (**Figures 2-1** and **2-2**). This translates to a total of 39 million and 43.5 million acres treated with thiamethoxam and clothianidin, respectively. **Figures 2-1** and **2-2** also depict the estimated annual acres treated of crops receiving foliar or soil applications. For both clothianidin and thiamethoxam, the majority of acres treated via foliar or soil applications are represented by cotton.

Table [STYLEREF 1 \s]-[SEQ Table * ARABIC \s 1]. Estimated acres treated with thiamethoxam or clothianidin via seed treatment.

Crop	US Bearing Acreage (USDA 2017)	Thiamethoxam				Clothianidin			
		PCT (annual average)	PCT (annual max)	Average acres treated	Maximum acres treated	PCT (annual average)	PCT (annual max)	Average acres treated	Maximum acres treated
Corn	87,668,000	25	45	21,917,000	39,450,600	45	65	39,450,600	56,984,200
Soybeans	75,869,000	15	25	11,380,350	18,967,250	<2.5	<2.5	<1,896,725	<1,896,725
Cotton	7,664,400	30	45	2,299,320	3,448,980	<2.5	<2.5	<191,610	<191,610
Wheat	45,157,000	5	15	2,257,850	6,773,550	<2.5	<2.5	<1,128,925	<1,128,925
Sorghum	6,910,000	20	25	1,382,000	1,727,500	5	15	345,500	1,036,500
Potatoes	1,052,000	15	20	157,800	210,400	NA	NA	NA	NA
Sugar beets	1,154,200	5	10	57,710	115,420	40	55	461,680	634,810

NA = not available

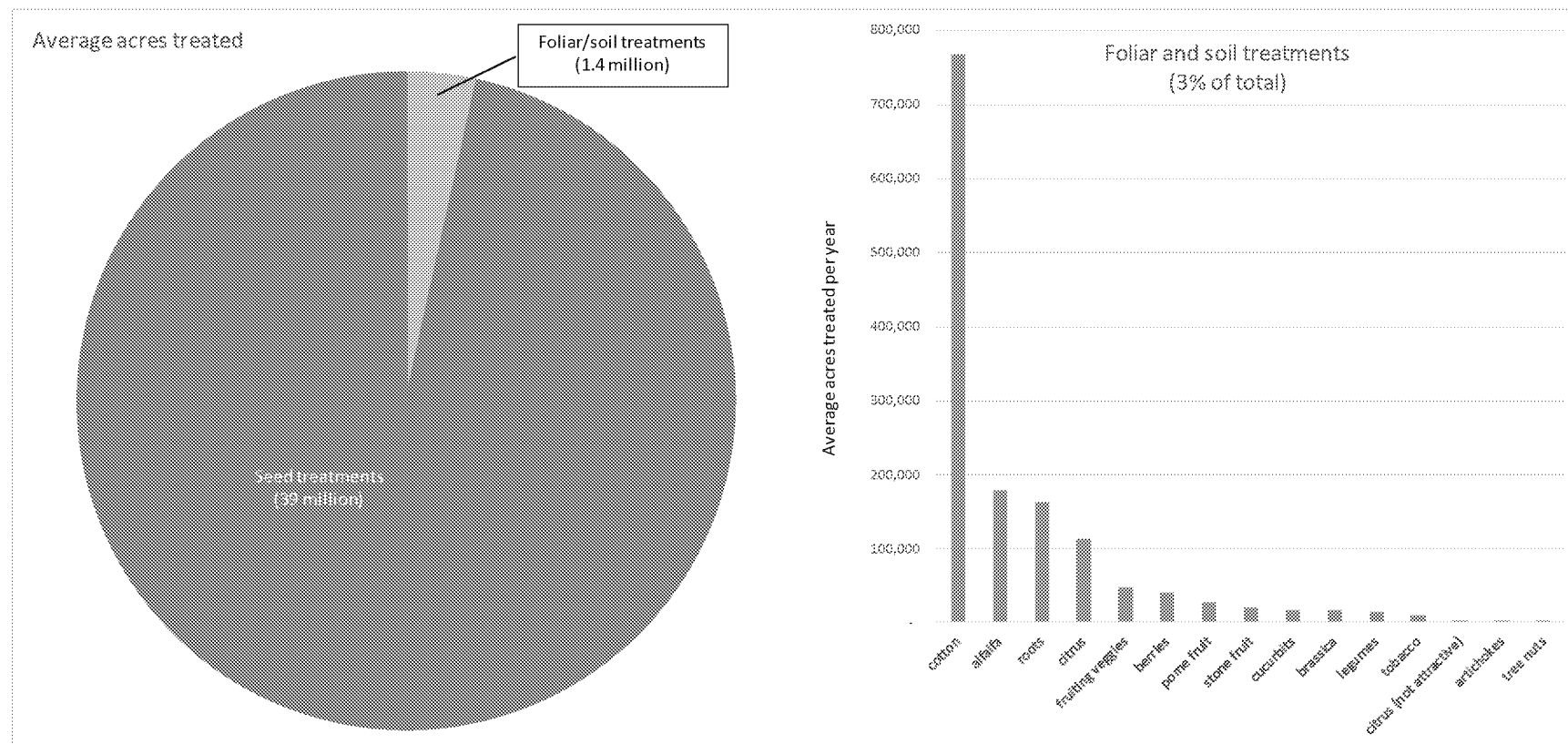


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]. Average acres treated of thiamethoxam in the US per year.

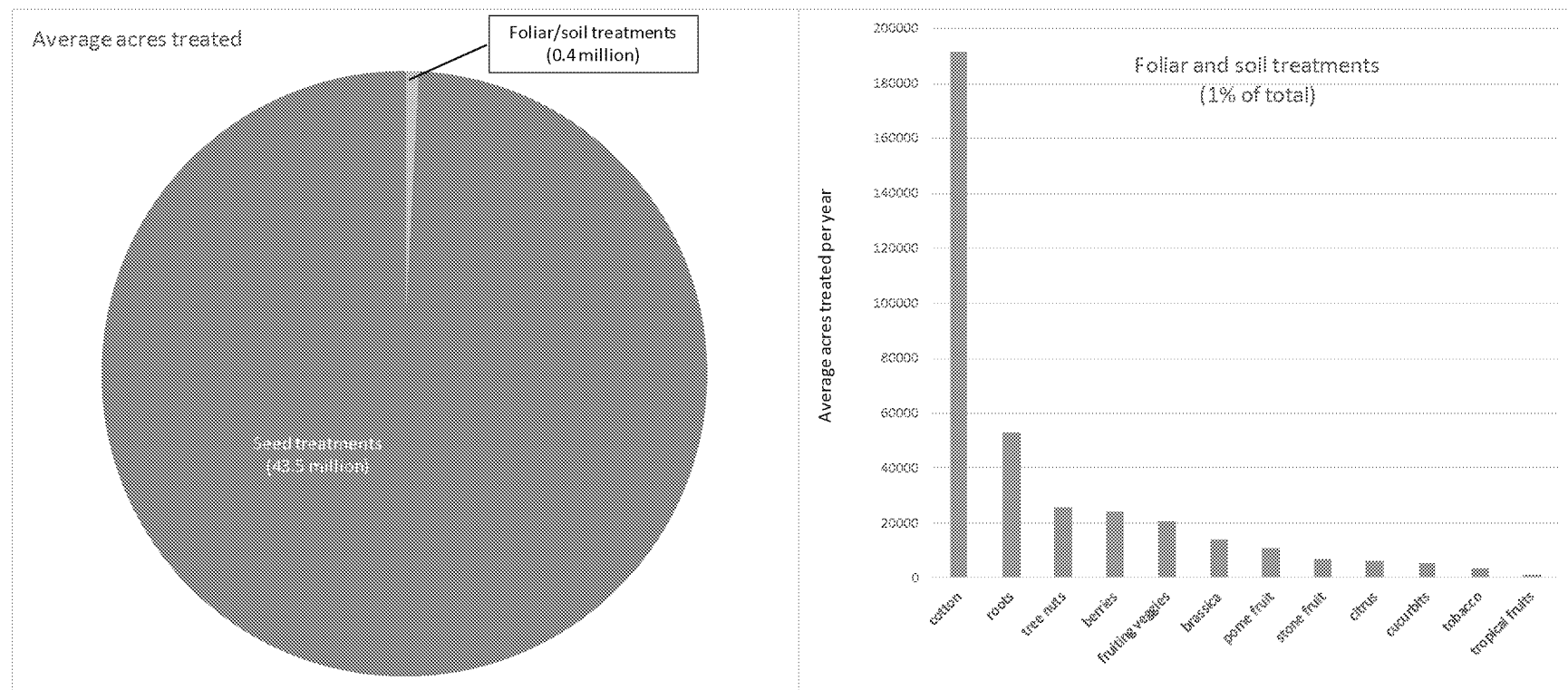


Figure [STYLeref 1 \s]-[SEQ Figure * ARABIC \s 1]. Average acres treated of clothianidin in the US per year.

2.5 Overview of Physicochemical, Fate, and Transport Properties

Clothianidin and thiamethoxam have similar physical/chemical properties (Table 2-9). They are a highly water soluble, with low vapor pressure, low Henry's Law Constants and low octanol-water partition (K_{ow}) coefficients. These properties suggest that the chemicals will be readily soluble for movement with water, and that it is unlikely that they will volatilize to a meaningful degree. In addition, their organic carbon partition coefficient (K_{oc}) values indicate that they are mobile to moderately mobile in soil.

The dominant transformation process for both clothianidin and thiamethoxam is photolysis (days to weeks in water; months in soil). While photodegradation may occur on soil surfaces following soil application and on wet foliage in the case of foliar application, photolysis on dry soil appears to be slower. Aerobic soil transformation for both clothianidin and thiamethoxam is comparatively slow (half-life values are on the order of months to more than a year); therefore, both compounds are expected to persist in the soil system.

Clothianidin and thiamethoxam are xylem and phloem- mobile systemic compounds in plants and are readily taken up by the roots of the plant and translocated throughout the plant via the transpiration stream. The available fate studies for thiamethoxam indicate that clothianidin is not a major degradate in abiotic metabolism (i.e., hydrolysis, photolysis) or aqueous and soil metabolism studies. The available plant metabolism and residue studies do show clothianidin formed as a major degradate. This suggests that thiamethoxam is metabolized within plants to form clothianidin.

Table [STYLeref 1 \s]-[SEQ Table * ARABIC \s 1]. Comparison of physical, chemical and fate properties of clothianidin and thiamethoxam

Parameter (units)	Clothianidin (MRID #)	Thiamethoxam (MRID #)
Formula	$C_6H_8ClN_5O_2S$	$C_8H_{10}ClN_5O_3S$
Molecular weight (g/mol)	249.7 (44703304)	291.7 (44703304)
Water solubility (mg/L)	327 (@20°C) (44703305)	4100 (@25°C) (44703305)
Vapor pressure (mm Hg)	2.9×10^{-13} (@20°C) (44703305)	4.95×10^{-11} (@25°C) (44703305)
Henry's law constant (atm m ³ /mol)	2.9×10^{-16} (calculated)	4.62×10^{-15} (calculated)
Octanol-water partition coefficient (K_{ow})	13 (44703305)	0.74 (44703305)
Soil partition coefficient (K_{oc} ; L/kg _{oc})	84 (sandy loam) 119 (sand) 123 (clay loam) 129 (loamy sand) 345 (sandy loam) (4542231111)	33.1 (silty clay loam) 38.3 (loam) 43.0 (sand) 53.1 (loam) 77.2 (sandy clay loam) 176.7 (sandy loam) (44703502)
Hydrolysis half-life (days)	Stable (at pH 5,7,9) (45422317)	Stable (at pH 5 and 7) 4.2, 8.4 (at pH 9) (44703416, 44703417)

Aqueous Photolysis half-life (days)	14.4 (45422318-22)	2.3, 3.1 (44715024, 44715025)
Soil Photolysis half-life (days)	34 (45422323)	79, 97 (44715027, 44715028)
Aerobic soil metabolism half-life (days)	148 – 1155 (45422326-28)	101 – 353 (44703419, 44703501, 44703418)
Anaerobic aquatic metabolism half-life (days)	27 (45422330)	25.3, 28.6 (44715029, 44715030)
Terrestrial field dissipation half-life (days)	277 – 1386 (45490703-05; 45422331-36; 45422508; 45422604; 45422612)	1.1 - 111 (44703505, 4727506, 44948902, 44948903 44975401)

2.6 Stressors of Toxicological Concern

When assessing the ecological risks of a pesticide active ingredient, EFED considers degradates that are of similar or greater toxicity compared to the parent. For this assessment, stressors of concern for applications of thiamethoxam include both thiamethoxam and its major degradate clothianidin. The only stressor of concern for applications of clothianidin is clothianidin itself. Available fate studies for clothianidin have identified desmethyl clothianidin (N-(2-chloro-5- thizolylmethyl)-N'-nitroguanidine; (TZNG)) as a major degradate; however, available honey bee data suggest that TZNG is orders of magnitude less toxic to adult honey bees on an acute oral exposure basis (TZNG LD50 = 3.95 µg a.i./bee (MRID 45422430); clothianidin LD50 = 0.0037 µg a.i./bee (MRID 45422426)). Therefore, TZNG is not considered a residue of concern for this assessment.

- For this risk assessment, the following total residue approach is used for thiamethoxam to account for its metabolism to clothianidin:
- It is assumed for the purposes of this assessment that thiamethoxam and clothianidin are of similar toxicity to individual bees. This is supported by available toxicity data (discussed in **Section 4**) using laboratory studies (Tier I). Consequently, endpoints are compared to total residues as below:
 - Residues are summed (using molar equivalents) to represent total thiamethoxam and clothianidin exposure. Exposure is expressed as clothianidin-equivalents (c.e.). In this approach, thiamethoxam exposure and effects data are converted to clothianidin equivalents by multiplying the thiamethoxam values by 0.856, which is the ratio of the molecular weights of clothianidin to thiamethoxam.
- The available colony feeding study (Tier II) data suggest honeybee colonies are less sensitive to thiamethoxam than to clothianidin. However, this is more likely an artifact of dose spacing and inherent variability in field studies rather than significant differences in toxicities between the two chemicals.
 - For evaluating colony-level risk to bees, residues of clothianidin are summed (using molar equivalents) with thiamethoxam residues similar to Tier I analysis. However, both thiamethoxam and clothianidin endpoints are used to characterize risk based on the effect levels at similar doses. Exposures and endpoints are again expressed as clothianidin-equivalents (c.e.)

2.7 Protection Goals and Assessment Endpoints

The Agency has defined protection goals for assessing pesticide risks to bees; these goals include: 1) maintenance of pollination services; 2) ensuring hive product production (*e.g.*, honey, wax, propolis); and, 3) ensuring bee biodiversity (**Table 2-10**; USEPA *et al.* 2014). While these goals do not apply uniformly across *Apis* and non-*Apis* bees, they are considered protective for social and solitary bees, where honey bees are generally used a surrogate for non-*Apis* bees. These protection goals in turn influence assessment endpoints and their associated measurement endpoints.

The protection (or management) goals, assessment endpoints and measurement endpoints identified in **Table 2-10** reflect the Agency's use of honey bees as a surrogate for other bees. Although this approach has limitations, it is assumed that data on individual bees (*i.e.*, adult or larva) as well as colony-level data can provide relevant information on the potential effects of a pesticide on both solitary bees as well as social bees. In addition, protection of honey bees contributes to pollinator diversity directly and indirectly, by protecting pollination services and propagation of the many plant species pollinated by bees. Honey bees are considered the most important commercial pollinators in the U.S. and abroad and in evaluating potential risks specific to honey bees, the protection goals of preserving pollination services and production of hive products (*e.g.*, honey, wax) are readily assessed through the assessment of bee population size (colony strength measured in terms of the number of adult bees and developing young [brood]) and the stability (*e.g.*, presence of a queen, uniform brood pattern) of the colony and through direct and indirect measures of the quantity and quality of hive products. As such, the sensitivity of individual larval or adult honey bees based on laboratory-based acute and chronic toxicity studies serve as reasonable measurement endpoints for screening-level assessments of the potential for adverse effects on colony strength, survival and capacity of the colony to produce any products following exposure to a pesticide. While these measurement and assessment endpoints are evaluated using managed honey bee colonies, they apply to feral honey bee colonies and, in the absence of data specific to other bees, these data provide useful information for assessing the survival and development of solitary and social non-*Apis* bees and potential effects on bee species richness and biodiversity. To the extent that data are available for other social non-*Apis* bee species (*e.g.*, the bumble bees) and solitary non-*Apis* bees (*e.g.*, mason bees (*Osmia lignaria*), and alfalfa leaf-cutting bee (*Megachile rotundata*)) the potential for adverse effects on these bees from exposure to clothianidin and thiamethoxam is also be evaluated.

Table [STYLeref 1 \s]-[SEQ Table * ARABIC \s 1]. Protection goals and examples of associated assessment and measurement (population and individual) endpoints for honey bees (*Apis mellifera*) and non-*Apis* social and solitary bees.

Protection Goal	Assessment Endpoints	Example Measurement Endpoints	
		Population level and higher	Individual Level
Contribution to Bee Biodiversity	Species richness ¹ and abundance	Individual bee survival (solitary bees) and colony strength and survival (social bees) Species richness and abundance ¹	Individual worker and larval survival assays; larval emergence; queen fecundity/reproduction

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Protection Goal	Assessment Endpoints	Example Measurement Endpoints	
		Population level and higher	Individual Level
Provision of Pollination Services	Population size ² and stability of native bees and commercially managed bees	Colony strength and survival; colony development	Individual worker and larval survival assays; queen fecundity; brood success; worker bee longevity
Production of Hive Products	Quantity and quality of hive products	Quantity and quality of hive products; including	Individual worker and larval survival assays;

¹ Use of honey bees as a surrogate for other insect pollinators has limitations; however, it is assumed that as with all surrogates, data on individual organisms as well as colony-level data would provide relevant information on the potential effects of a pesticide on both solitary as well as social non-Apis bees. In addition, protection of honey bees contributes to pollinator biodiversity indirectly by protecting pollination services and propagation of the many plants species requiring insect pollination.

² For managed honey bees, population size can include numbers of colonies.

2.8 Conceptual Models and Risk Hypotheses

The risk hypothesis and conceptual model identify the source of the stressor, route of exposure, biological receptor, and changes in the receptor attribute(s) of concern (USEPA, 1998). For clothianidin and thiamethoxam, the conceptual models are depicted separately for each method of application to agricultural crops (foliar spray, soil application, and seed treatment).

2.8.1 Foliar Spray

There are many factors that determine the exposure of bees to a pesticide, including methods and timing of application, application rate, attractiveness of the crop to bees, and agronomic practices such as harvesting crops prior to bloom. In general, however, foliar application of systemic pesticides such as clothianidin and thiamethoxam are expected to result in exposure of bees via two dominant routes: 1) direct contact via interception of suspended pesticide droplets and recently-sprayed surfaces; and, 2) ingestion of pesticide residues in pollen and nectar (**Figure 2-3**). With foliar sprays, these routes of exposure may occur on the treated field or adjacent to the treated field due to spray drift. With honey bees, nectar and pollen foragers are expected to receive exposure via their frequent interaction with blooming crops. Dominant exposure routes of in-hive bees (*e.g.*, nurse bees) include ingestion and processing of pollen and nectar and exposure through contact with comb wax. Stored honey is expected to be a potential route of exposure for bees. Processed bee bread (combination of honey and pollen) and are major routes of exposure for developing larvae. For the queen, royal jelly is the major route of exposure, although limited evidence suggest pesticide levels in royal jelly are orders of magnitude below those found in pollen and nectar (USEPA 2012).

Exposure of honey bees to clothianidin or thiamethoxam in the vapor phase is not expected to be a significant route of exposure, regardless of application method, due to their low vapor pressure values (**Tables 2-8 and 2-9**). Exposure of honey bees through contact with contaminated soil is also not expected to be a major route of exposure, although this may be an important route of exposure for ground-nesting bees on or near the treated site. Other routes of exposure are also possible, including consumption of

plant guttation fluids (xylem water exuded from the plant), water from dew droplet formation on leaves, puddles, and surface water. Although relatively high concentrations of neonicotinoid insecticides have been reported in plant guttation fluid (e.g., Girolami *et al.* 2009), a review of honey bee exposure routes indicated high uncertainty in the importance of guttation fluid ingestion relative to other oral routes of exposure (e.g., nectar and pollen; USEPA 2012). This uncertainty is partly due to the availability of guttation fluid at times of the year when crops are generally unattractive to pollinators and other sources of water are available (Godfray *et al.* 2014; USEPA 2012). Furthermore, there is presently a lack of robust information on water intake rates by bees from surface water and multiple factors that affect these rates. Therefore, this pathway is currently under investigation by USEPA and is not considered for quantitative estimation of risk to bees.

Changes in the assessment endpoints (e.g., size and stability of bee colonies, production of hive products, pollinator species richness and abundance) as a result of the aforementioned pesticide exposure routes may occur through various means, including reduction in number of worker bees available for foraging or maintaining hive temperature (overwintering), reduction in foraging efficiency via sub-lethal effects on workers, decreased number or delayed development of brood either from direct exposure to pesticide or indirectly from reduced brood feeding and maintenance by hive bees, and reduced fecundity and survival of queens. Changes in these assessment endpoints are directly related to impacts on protection goals of maintaining pollination services, production of hive products and contribution to pollinator biodiversity.

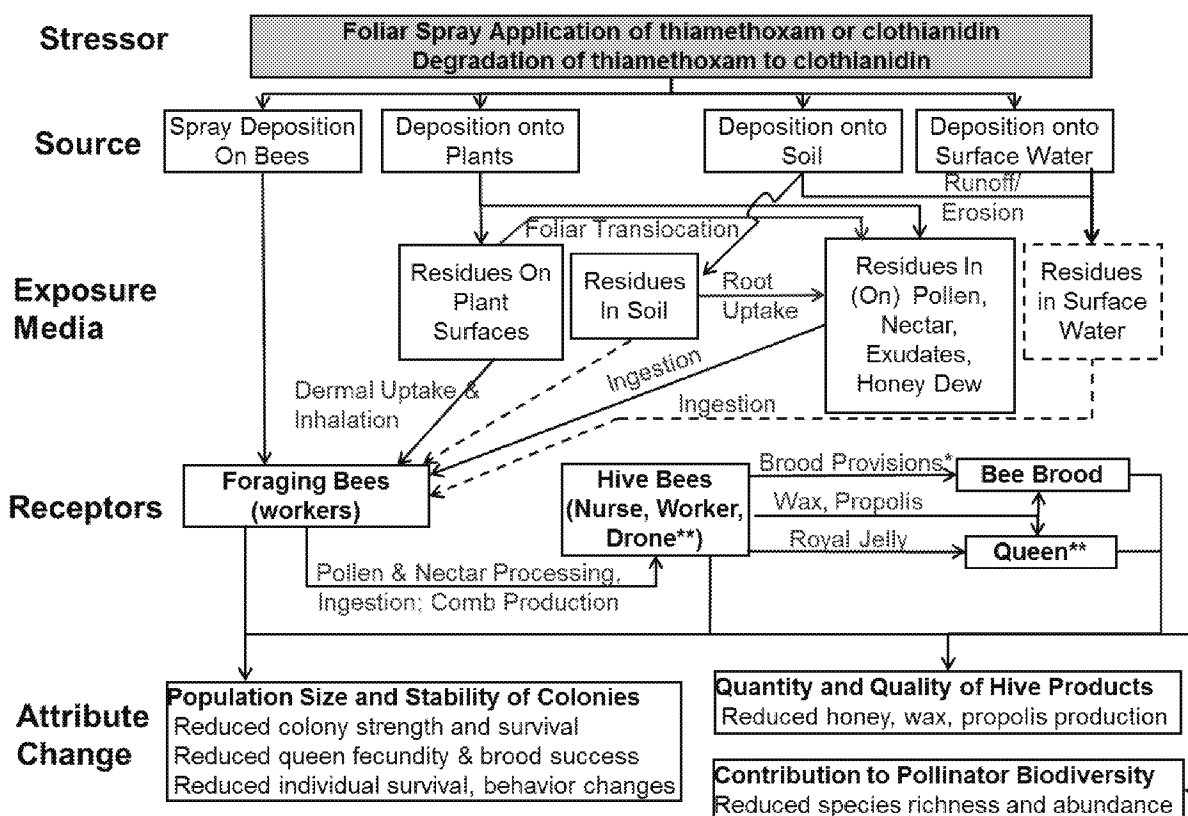


Figure [STYLeref 1 \s]-[SEQ Figure * ARABIC \s 1]. Conceptual model for risk assessment of foliar spray applications of clothianidin and thiamethoxam to honey bees. Dashed lines not considered to be major routes of exposure.

2.8.2 Soil Application

Exposure of honey bees to clothianidin and thiamethoxam via soil applications (*e.g.*, drench, injection, in-furrow sprays and chemigation) are expected to follow the same routes of exposure as discussed above for foliar sprays, except that contact exposure (on-field and off-field) is not expected to be significant since applications are made at or near planting when crops are not considered attractive to bees (**Figure 2-4**). Furthermore, the nature of these applications is not expected to result in substantial spray drift to adjacent sites relative to foliar sprays. Depending on the timing of rainfall events, there is some potential for exposure via clothianidin and thiamethoxam runoff to areas immediately adjacent to the treated field where residues could be taken up by pollinator-attractive plants. Also, given their persistence in soil, there is potential for soil applications of clothianidin and thiamethoxam to be taken up by rotational plants (*e.g.*, cover crops) that are planted after crop harvest. Some of these rotational crops may be attractive to bees as sources of pollen and/or nectar (*e.g.*, clover).

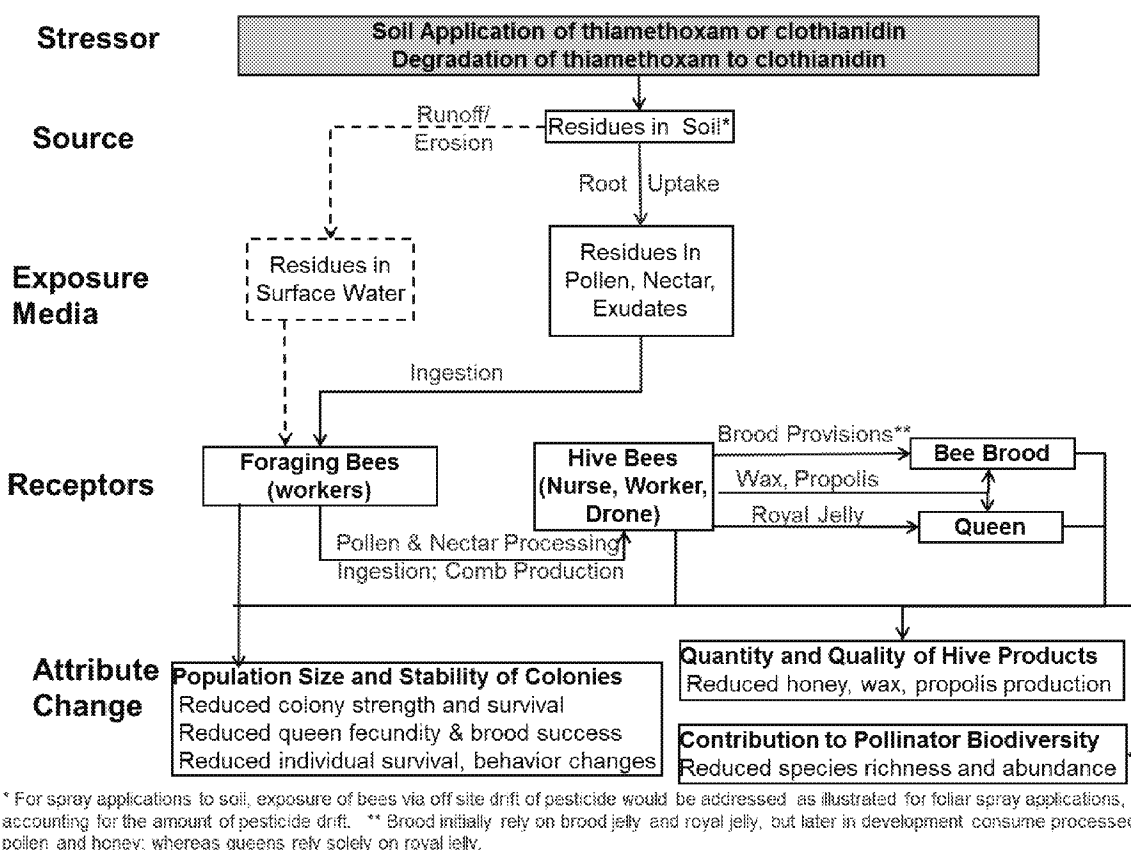


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]. Conceptual model for risk assessment of soil applications of clothianidin and thiamethoxam to honey bees. Dashed lines not considered to be major routes of exposure.

2.8.3 Seed Treatment

Potential exposure routes of honey bees to clothianidin and thiamethoxam used as seed treatments include pollen, nectar, exudates (*e.g.*, guttation fluid), and honey dew resulting from translocation from the seed to growing plant tissues (**Figure 2-5**). Another important route of exposure includes contact with abraded seed coat dust during planting has been the focus of considerable research (*e.g.*, Tapparro *et al.* 2012, Krupke *et al.* 2012). This pathway has been associated with numerous incidents of honey bee mortality from mortality of foraging bees but not necessarily involving outright loss of the colony (Pistorius *et al.* 2009, Forster *et al.* 2009). The extent to which honey bees are exposed via contact with abraded seed coat dust is influenced by many factors including the physio-chemical properties of the seed coating, seed planting equipment, use of seed lubrication agents (*e.g.*, talc), environmental conditions (wind speed, humidity), and hive location in relation to sowing and prevailing winds. Off-site drift of contaminated seed coat dust can contribute to residues on plants, soil, and surface water to which bees may be exposed through direct contact and ingestion of surface water, pollen, and nectar. One important attribute of the overall seed treatment exposure pathway is that exposure to pesticides may occur over a wide time scale (*e.g.*, at seed sowing, during plant growth and flowering *etc.*).

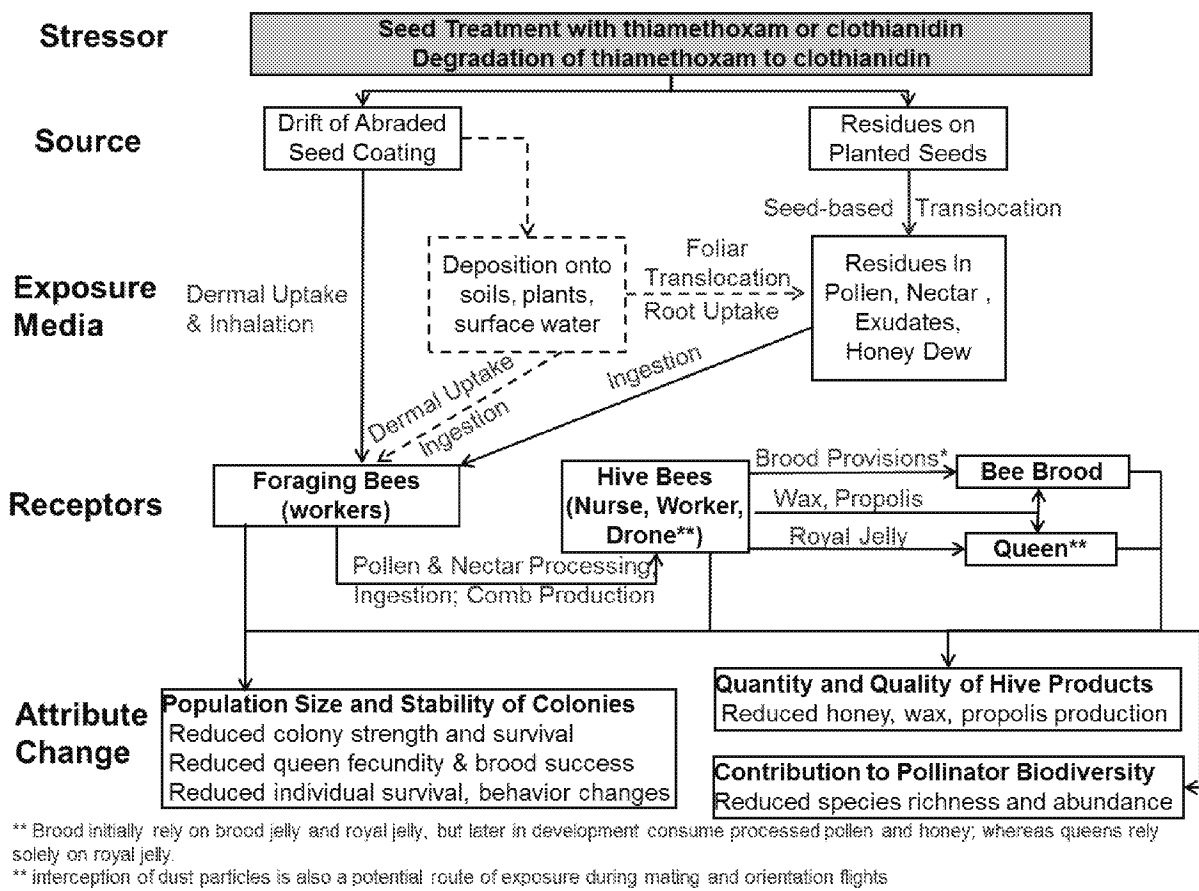


Figure [STYLeref 1 \s]-[SEQ Figure * ARABIC \s 1]. Conceptual model for risk assessment of planting of clothianidin or thiamethoxam -treated seeds to honey bees

2.9 Analysis Plan

The analysis plan articulates data gaps, the methods used to evaluate existing and anticipated data, and the assumptions that were made where data are missing. The analysis plan also identifies the specific measures of exposure (*e.g.*, estimated environmental concentrations; EECs) and effect (*e.g.*, median lethal dose for 50% of the organisms tested; LD50) which will be used to develop risk estimates.

2.9.1 Measures of Exposure

The primary routes of exposure being assessed quantitatively are the contact and oral routes. These are considered the dominant exposure routes for clothianidin and thiamethoxam. Measures of contact exposure include the estimated contact dose on a per bee basis (*e.g.*, $\mu\text{g a.i./bee}$). Contact exposure is also incorporated into Tier II semi-field (tunnel) studies, although rarely quantified on a per bee basis. Oral exposure is also determined on a mass of active ingredient per bee basis and considers ingestion of contaminated pollen and nectar. The BeeREX¹² tool is used to provide estimates of pesticide exposures via contact and diet. When empirically based data are available for a crop, measured concentrations in pollen and nectar are used *in lieu* of BeeREX default estimates of dietary exposure. Detailed methods for estimating exposure to honey bees are described later in **Section 3**.

At Tier I, pesticide EECs are estimated based on honey bee workerlife stages with known high-end consumption rates. For larvae, food consumption rates are based on 5-day old larvae, which consume the most food compared to other days of this developmental stage. For adults, the screening method relies upon nectar foraging bees, which consume the greatest amount of nectar of all castes while nurse bees (young, in-hive females) consume the greatest amount of pollen. It is assumed that this value will be comparable to the consumption rates of adult males (drones) and will be protective for adult queens as well (USEPA, 2012; USEPA, 2014). Although the queen consumes more food than adult workers or drones, the queen consumes “processed” food (*i.e.*, royal jelly produced by the hypopharyngeal glands of nurse bees) that is assumed, based on currently available data (CFS data, also USEPA, 2012), to contain orders of magnitude lower pesticide residues than the unprocessed nectar and pollen consumed by adult workers.

Nectar is the major food source for forager honey bees as well as nurse bees. Therefore, ingestion of pesticide residues in nectar likely represents the predominant route of exposure for bees. However, when pesticide concentrations in pollen are much greater than in nectar or for crops that mainly provide pollen to bees, exposures to nurse bees, which consume more pollen than any other adult honey bees, is considered on a case-by-case basis. In fact, Bee-REX allows calculation of exposure and resulting risk quotients (RQs) for all types of bee castes. As described in the 2012 White Paper (USEPA *et al.* 2012) presented to the FIFRA Scientific Advisory Panel and the final Guidance Document for Assessing Risk to Bees (USEPA *et al.* 2014), for dietary exposure from foliar applications, it is assumed that pesticide residues on tall grass (from the Kenaga nomogram of T- REX which is incorporated into Bee-REX) are suitable surrogates for residues in pollen and nectar of flowers that are directly sprayed. Where available for a given crop group, empirical residue data in pollen and nectar is used in Bee-REX to generate refined Tier I

¹² <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#terrestrial>

RQs. The Bee-REX model is a screening-level tool that is intended for use in a Tier I risk assessment to assess exposures of individual bees to pesticides and to calculate risk quotients; however, Bee-REX is not intended to assess exposures and effects at the colony-level (*i.e.*, for honey bees).

The Tier I exposure assessment is intended to account for the major routes of pesticide exposure that are relevant to bees (*i.e.*, through diet and contact). Exposure routes for bees differ based on application type. In the model, bees foraging in a field treated with a pesticide through foliar spray could potentially be exposed to the pesticide through direct spray as well through consuming contaminated food. For honey bees foraging in fields treated with a pesticide through direct application to soil (*e.g.*, drip irrigation), through seed treatments, or through tree injection, direct spray onto bees (*i.e.*, contact exposure) is not expected. For these application methods, pesticide exposure through consumption of residues in nectar and pollen are expected to be the dominant routes.

In the Tier II assessment, the maximum mean measured residues in nectar are compared to endpoints from colony-level studies where endpoints are expressed in terms of the concentration in spiked sucrose solution diet. This exposure route considers exposure from consuming contaminated sucrose (*i.e.*, nectar) but does not consider exposure via consumption of contaminated pollen. This assessment differs from the preliminary assessment (USEPA 2017) in the way exposure is estimated via consumption of contaminated pollen. The previous assessment considered exposure via contaminated nectar separately from consumption of contaminated pollen in bee bread¹³ (measured). This assessment replaced that method of evaluating exposure using a combined total dietary approach which takes the measured values of pollen and nectar in single crop and adjusts the concentration based on relative consumption rates for a single estimated dietary dose. Details on this method are presented in **Attachment 1**.

As mentioned above, In the Tier II assessment, exposures are estimated using the maximum mean measured residues in pollen and nectar, summing them (to get a total nectar exposure value) and then comparing these values to endpoints from colony-level studies expressed in terms of the concentration in spiked sucrose solution diet. This necessitates a data set of empirical residue values from specific crops available to compare to colony effect levels. As part of the Registration Review of the nitroguanidine-substituted neonicotinoid insecticides (*i.e.*, imidacloprid, clothianidin, thiamethoxam, dinotefuran), EPA required technical registrants submit data on the concentrations of these compounds and their residues of concern in bee-relevant matrices¹⁴. While these individual chemical data sets are expansive, it is not feasible to perform trials to capture residues for all registered crops. Thus, for Tier II analysis, this assessment uses a Residue Bridging approach to supplement, and in the cases where no chemical specific data available act as a surrogate for, empirical residue data in pollen and nectar. An overview of how this methodology is incorporated into the Tier II risk assessment is provided in **Section 2.11** below with full details on this method and the results presented in **Attachment 2**.

Bees may also be exposed to pesticides via other routes of exposure such as through plant guttation fluid, surface water, soil (for ground nesting bees) and drift of abraded seed coat dust. As noted previously, the extent to which bees are exposed via plant guttation fluids and surface water is uncertain. Furthermore,

¹³ Since bee bread is a combination of pollen and honey (Winston 1987), it is necessary to weight the empirical residues in pollen and nectar (from crops) based on their relative contributions in bee bread. Details on this method can be found in the preliminary assessment.

¹⁴ The registrants also submitted residue data for other matrices that could potentially be used as surrogates for pollen and nectar (*e.g.*, anthers, flowers, leaves).

the Agency currently lacks reliable methods for evaluating these exposure routes in a quantitative manner (*i.e.*, derivation of Tier I EECs that consider bee-specific drinking water consumption). Therefore, consistent with the Agency's 2014 risk assessment guidance, this risk assessment focuses on estimates of exposure via contact and ingestion of residues in pollen and nectar routes only. Although exposure and effects to bees via exposure to abraded seed coat dust has been documented, these data are highly variable and methods are not currently available to provide reliable estimates for this route of exposure. The Agency continues to work with stakeholders to mitigate the potential for adverse effects on bees from this exposure pathway through best management practices and the development of alternative technologies to reduce dust off during planting (*e.g.*, alternative lubricants, equipment modifications, etc.)¹⁵

2.10 Measures of Effects

The primary species of focus in this risk assessment is the honey bee. This focus reflects the dominant role this species has in managed pollination services for agricultural crops throughout the U.S. The focus on *A. mellifera* also reflects the availability of standardized methods for estimating exposure and effects on this species. This assessment considers a variety of measurement endpoints for quantifying risk to honey bees; these endpoints differ according to the level of biological organization being assessed. At the Tier I (organism) level, measures of effects include:

- The acute contact lethal dose to 50% of the individual adult worker bees tested (*i.e.*, LD50)
- The acute oral LD50 to adult worker bees,
- The acute LD50 to larval bees,
- The chronic (10-d) oral no-observed adverse effect level (NOAEL) for adult worker bees, and
- The chronic (21-d) NOAEL for larval bees, which extends through adult emergence.

The acute and chronic toxicity endpoints for Tier I studies are derived from standardized laboratory toxicity tests conducted according to Office of Chemical Safety and Pollution Prevention (OCSP) and the Organization for Economic Cooperation and Development (OECD) guidelines¹⁶. For acute and chronic (adult) tests, lethality is the primary test endpoint, although sub-lethal effects are commonly noted; for

¹⁵ [HYPERLINK "http://www2.epa.gov/pollinator-protection/2013-summit-reducing-exposure-dust-treated-seed" \h]

¹⁶ https:[HYPERLINK

"http://www.oecd.org/env/ehs/testing/Draft%20TG%2010d%20Honeybee%20feeding_Feb%202016.pdf" \h]w[HYPERLINK

"http://www.oecd.org/env/ehs/testing/Draft%20TG%2010d%20Honeybee%20feeding_Feb%202016.pdf" \h]

⁸https:[HYPERLINK

"http://www.oecd.org/chemicalsafety/testing/Draft_GD_honeybee_larval_tox_repeated_exposure_25_February" \h]w[HYPERLINK

"http://www.oecd.org/chemicalsafety/testing/Draft_GD_honeybee_larval_tox_repeated_exposure_25_February" \h]_2014.pdf

chronic larval tests, the primary measurement endpoints are larval survival (Days 8), pupal survival (Day 15), and adult emergence (on Day 22).

At the Tier II and Tier III levels, measures of effect at the colony level typically include:

- forager bee mortality;
- queen fecundity (*e.g.*, eggs production);
- brood (egg, larvae, pupae) development and survival;
- colony weight, strength and survival;
- adult foraging activity; and,
- quantity and quality of food provisions

These effects may be expressed in terms of a particular pesticide application rate (*e.g.*, lbs. a.i./A) or the concentration of the active ingredient in the diet (*e.g.*, µg a.i./L in sucrose). As discussed in the 2014 Guidance (USEPA *et al.* 2014), other sub-lethal measurement endpoints such as proboscis extension reflex (PER), histopathological effects, and behavior anomalies are not considered as regulatory endpoints by themselves. However, to the extent that these effects contribute to impairment of the aforementioned colony-level effects, they are qualitatively characterized in the risk assessment.

Although the focus of this risk assessment is on the honey bee, the Agency recognizes that numerous other species of non-*Apis* bees occur in North America and that these bees have ecological and in some cases, commercial importance. For example, several species of non-*Apis* bees are commercially managed for their pollination services, including bumble bees (*Bombus spp.*), leaf cutting bees (*Megachile rotundata*), alkali bees (*Nomia melanderi*), and mason bees (*Osmia lignaria*), and the Japanese horn-faced bee (*Osmia cornifrons*). Importantly, non-*Apis* bees play an important role in crop and native plant pollination, besides their overall ecological importance in contributing to biological diversity. Although standard methods are currently not available to quantitatively assess both exposure and effects to non-*Apis* bees, this assessment includes data on the effects of clothianidin and thiamethoxam to non-*Apis* bees and qualitatively assesses the potential for adverse effects on non-*Apis* bees from exposure to residues resulting from the registered uses of these compounds.

Multiple factors can influence the strength and survival of bees whether they are solitary or social. These factors, including disease, pests (*e.g.*, mites), nutrition, bee management practices, and weather can confound the interpretation of studies intended to examine the relationship of the test chemical to a receptor (*i.e.*, larval or adult bee). Therefore, most studies attempt to minimize the extent to which these other factors impact the study; however, higher-tier studies afford less control over these other factors, and their role may become increasingly prominent as the duration of the study is extended. Although studies attempt to minimize the confounding effects of other environmental factors, there is uncertainty regarding the extent to which the effects of a chemical may be substantially different had these other factors been in place.

2.11 Higher Tiered analysis for honey bees (*Apis* sp.)

A Tier II analysis was conducted for those crops where the Tier I refined analysis indicated potential risk (*i.e.*, acute or chronic risk LOCs were exceeded for one or more honey bee age groups). This analysis involved

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comparison of concentrations in pollen and nectar to honey bee colony level endpoints. This section provides greater detail on the conduct of the Tier II level risk assessment for clothianidin and thiamethoxam and further describes additional factors considered to derive the final risk conclusions from clothianidin or thiamethoxam exposure following seed treatment and foliar and soil applications.

An uncertainty associated with this approach and the reliance on the sucrose based CFS endpoints relates to the interpretation of Tier 2 effects based on the 6-week exposure. In considering exposure, this approach assumes that bees forage on the treated crop nearly 100% of the time to represent the nectar needs of the colony. In the field, bees may forage for significantly shorter periods of time particularly for crops such as cherries and blueberries that have a 2-3 weeks blooming duration. Bees may also forage on alternative (untreated) plants. Conversely, bees associated with migratory colonies used for pollination services may feed on treated crops for similar or possibly longer periods of time over the course of a growing season. The conservative assumptions are considered for foliar and soil applications, where exposures exceed CFS endpoints. Specifically, the analysis considers the relative difference of the exposure to the endpoint, which can be interpreted as the amount of dilution (from non-contaminated sources of food) that would still result in exposures that pose a risk to the colonies. In the sucrose-based CFS for clothianidin and thiamethoxam, some effects were observed at CCAs (Colony Condition Assessments) that occurred within the exposure window (*i.e.*, approximately 3 weeks of exposure), suggesting that effects could occur after <6 weeks.

2.11.1 Tier II methodology

Exposure to hives was based on empirical residues in pollen and nectar for specific crops. In several cases, concentrations available for a different chemical or crop were “bridged” to either clothianidin or thiamethoxam and the crop of interest to the assessment. A detailed analysis and bridging approach for the available crop residue data for clothianidin, dinotefuran, imidacloprid and imidacloprid from foliar and soil applications is provided in **Attachment 2**. **Attachment 3** includes an analysis of available non-agricultural (*i.e.* ornamental and turf (blooming weeds)) residue data. An analysis of the residue data and bridging approach for seed treatments is provided in **Attachment 4**.

2.11.1.1 Matrices considered in this assessment

As discussed in USEPA 2014, it is assumed that the predominant exposure routes for bees are through contact and diet. Worker honey bees consume pollen and nectar, with consumption rates that differ by their job in the hive. The tier I analysis indicated that bees are much more sensitive to clothianidin and thiamethoxam through diet, therefore, the Tier II assessment focuses on this route of exposure.

As indicated by USDA (2017) many of the crops registered by use of thiamethoxam and clothianidin produce pollen and nectar that are attractive to honey bees. some crops only produce either nectar or pollen that are attractive to honey bees (*e.g.*, cotton pollen is not attractive to honey bees; grapes do not produce attractive nectar).

In regard to nectar, this assessment focuses on floral nectar. Several plants are known to also produce extrafloral nectar (*e.g.*, via nectaries located on leaves and stems)¹⁷. The USDA Crop Attractiveness List

¹⁷ <http://www.extrafloralnectaries.org>

(USDA 2017) does not provide an account of the attractiveness of extrafloral nectaries to honeybees for most of the crops assessed here. Unlike floral nectaries which have evolved to promote plant pollination via bees and other organisms, extrafloral nectaries are generally believed to have evolved to attract arthropods (*e.g.*, ants, predatory wasps, etc.) for protection of the host plant from herbivory by other organisms (*e.g.*, Escalante-Pérez et al. 2012¹⁸). Therefore, the presence of extrafloral nectaries does not necessarily mean that honey bees are using the exudates of the nectaries as a food source; rather, but the potential attractiveness of extrafloral nectar cannot be excluded as a significant exposure source of bees. The extrafloral nectary, if attractive, may extend the potential window of exposure beyond the bloom period or result in differential exposure of honey bees as evidenced by the higher concentrations of some neonicotinoids in cotton extrafloral nectaries in comparison to the floral nectar concentrations. Of the crops with residue data, extrafloral nectar residues are only available for cotton. Given that honey bees have been observed visiting both floral and extrafloral sites on cotton plants (Allard 1911¹⁹) and the similarity of sugar content of floral and extrafloral nectar, it is assumed that honey bees will collect and consume both floral and extrafloral nectar from cotton plants. The extent to which bees collect either type of nectar is unknown.

2.11.1.2 Summary of foliar and soil bridging approach

Studies evaluated were from registrant submissions of unpublished data. Study designs varied among studies, with differences in application timing, number of samples collected, number of sampling periods, number of seasons, number of trials, and others. When considering the available data, the most robust data sets exist for the following crop groups and application methods:

- Cotton, foliar;
- Cucurbit, foliar and soil;
- Citrus, foliar (pre-bloom) and soil;
- Stone fruit, foliar (post-bloom);
- Berries, foliar (pre-bloom).

While many different factors may collectively influence neonicotinoid residues in pollen and nectar, not all of them can be reliably quantified for this residue bridging analysis, thus focus was on a subset of factors which can be readily quantified and evaluated based on the submitted data, including:

- Chemical;
- Crop;
- Plant matrix (pollen, nectar, flower);
- Season of application;
- Application site;
- Application method; and,
- Application timing.

These factors were evaluated using different methods, depending upon the available data. The overall methodology underlying the residue bridging analysis involved controlling for as many of the potentially confounding variables as possible (*e.g.*, application rate, application method, time between application and

¹⁸ Escalante-Pérez, M., Jaborsky, M., Lautner, S., Fromm, J., Müller, T., Dittrich, M., Kunert, M., Boland, W., Hedrich, R., Ache, P., 2012. Poplar Extrafloral Nectaries: Two Types, Two Strategies of Indirect Defenses against Herbivores. *Plant Physiol.* 159(3): 1176–1191.

¹⁹ Allard, H.A. 1911. Preliminary observations concerning natural crossing in cotton. American Breeders Association, Washington, D.C. p. 156-170

residue measurement, crop, *etc.*) and conducting appropriate statistical comparisons when sufficient data were available. This involved parametric or nonparametric methods of hypothesis testing or linear regression. In many cases, sufficient sample size was not available to conduct meaningful statistical comparisons. In these cases, a semi-quantitative approach was taken which included comparisons of the overlap in 95% confidence intervals or evaluation of cumulative frequency distributions. Comparison of residue levels among matrices identified the following general trends (for samples collected from the same studies and time points):

- Concentrations of residues of concern in are approximately an order of magnitude more than residues in nectar;
- Residue concentrations in pollen and anthers are similar, with residues in anthers tending to be somewhat lower than those in pollen (but within a factor of 4);
- Residue concentrations²⁰ in whole flowers are above those in nectar but are generally within a factor of 3.
- Residue concentrations resulting from foliar applications were generally much higher (orders of magnitude) than those from soil applications, especially for samples collected soon after application.
- When considering the different variables, the following influence residue levels: application method, application timing, and site; while no obvious influence can be determined for the remaining variables, *i.e.*, chemical or crop (within crop group). When considering crops outside of groups (*e.g.*, soybeans and melons), differences are observed in residues of different crops.

Crop groups used to establish tolerances were used here as a starting point for bridging purposes. In this analysis, residues of different individual crops within a crop group were compared to determine whether residues were representative of other crops within that group (*e.g.*, pumpkin and cucumber residues compared to determine representativeness of all cucurbits). The bridging analysis also compared crops from different crop groups (*e.g.*, almonds and peaches) to determine if residues could be bridged to crops outside of crop groups. In several cases, residues are bridged from crops outside of crop groups (*e.g.*, apple and orange foliar, pre-bloom application data bridged to all orchard crop groups).

The following groups had some residue data; however, the available data were deemed insufficient for representing their respective groups:

- Fruiting vegetables, foliar and soil.
- Root and tuber vegetables (foliar and soil);
- Legumes (foliar); and,
- Berries foliar (post-bloom) and soil.

In addition, there were no residue data for the following groups and application methods:

- Legumes (soil); and,
- Herbs and spices (foliar).

For these groups, available data from more robust data sets will be used based largely on botanical similarities. For (honeybee attractive) fruiting vegetables, (honeybee attractive) root and tuber vegetables, legumes, berries and herbs and spices, the available cucurbit and cotton data for the relevant application method were used as a surrogate. These crops were chosen since they are similar in form (*i.e.*, herbaceous for cucurbits, same taxonomic family for cotton's use as a surrogate for some okra and roselle in the fruiting vegetable crop group. For berries, orchard data are considered, as both groups include woody species. In the

²⁰ Except where otherwise stated in the analysis for specific commodities. For example, some berries did not observe this pattern and this was considered in the analysis of risk from applications to berries.

case of fruiting vegetables (and to some extent root and tuber) most crops in that analysis group are not considered honeybee attractive (USDA, 2018).

In cases where sufficient pollen and/or nectar residue data are not available for a given crop, data on residues in anthers may be used as a surrogate for pollen and data on residues in flower can be used as a surrogate for concentrations in nectar. It is recommended that anther data be used as a direct representative of pollen, with potential variability addressed by considering multiplying anther values by a factor of 3. For residues in flowers as a surrogate for nectar, concentrations in flowers are multiplied by a factor of 0.2 and 0.25 for foliar and soil applications, respectively, and flower concentrations are multiplied by a factor of 0.5 to determine pollen concentrations from both foliar and soil applications (with potential variability addressed by using empirical flower residues as an upper bound direct one-to-one surrogate for nectar and pollen). The rationale for the use of these surrogate matrices and their relationship to pollen and nectar is described in **Attachment 2**.

For residue data from foliar applications to cotton, cucurbits and berries, sufficient information were available in the studies to derive reliable residue decline curves. For those three groups, a Monte Carlo simulation was carried out where the dissipation rate constant and initial concentration were varied 1,000 times. Of those simulations, the 50th, 70th and 90th percentile residue decline curves are depicted to represent the median and higher bounds of potential exposure. These simulations are used below to characterize the duration of time where exposure exceeds colony level endpoints (*i.e.*, NOAEC and LOAEC values). For soil applications, dissipation rate constants could not be reliably derived even where robust datasets were available (*e.g.* cucurbits); therefore, a Monte Carlo simulation was not carried out for soil applications. In the case of pre-bloom foliar application residue data for orchard crops (apples and oranges), reliable dissipation rate constants could not be derived for the majority of the trials, so a Monte Carlo analysis was not conducted. When the available residue data were combined for apples and oranges, a dissipation curve could be reliably fit to the combined data, allowing for an estimate of the median residues over time and the duration of time exceeding colony level endpoints.

2.11.1.3 Summary of seed treatment bridging

Seed treatment residue data for corn, cotton, canola and soybean were considered sufficient for quantitative use. The bridging analysis discussed in detail in **Attachment 4** concludes that residues for a given crop can be bridged from one chemical to another. Comparison of residue data for the 4 crops suggests that crop may influence residue levels (residues in canola appear to be higher than the other three crops. However, concluding that there is a difference attributed to crops is uncertain due to the limited dataset for canola). Residue data for each crop were used to quantify residues for all chemicals with registered uses on that crop. All available residue data for seed treatments were combined and distributed to derive a general exposure level (90th percentile) for crops with no residue data.

2.11.1.4 Method for estimating total food exposures to colonies (nectar-equivalents)

Since honey bee colonies consume a combination of nectar and pollen, pesticide exposure should be assessed by considering both matrices. To assess exposure from total food, this method considers both the amount of each matrix consumed daily, as well as potential differences in toxicity to the colony that may be the result of different matrices. This “total food” method is based on a weight-of-evidence approach and considers colony biology and comparisons of available colony-level toxicity studies from sucrose and pollen patties.

The method for assessing exposure and potential risks to honey bee colonies involves estimating the total exposure of the pesticide through food. Since the sucrose-based CFSs are more robust (*i.e.* four sucrose-based CFS studies are available across both compounds, while only a single pollen-based CFS with less replication and no overwintering is available for clothianidin only) than the pollen-based studies, the exposure values are converted to a total nectar equivalent concentration ($C_{total-t}$; ng a.i./g) where $C_{total-t}$ is the sum of the concentration in nectar (at a given time), *i.e.*, $C_{nectar-t}$ (ng a.i./g), and the concentration in pollen at the same time, *i.e.*, $C_{pollen-t}$ (ng a.i./g). The concentration in pollen is adjusted by a weighting factor that accounts for the relative difference in pollen dose compared to nectar and possibly, any difference in toxicity between nectar and pollen. In this case we were able to conclude that exposure via nectar and pollen does not influence colony level toxicity as evidenced by comparable effects at similar consumed doses. The strength of this approach is that it integrates exposure from nectar and pollen, both of which are consumed daily by the colony.

This approach accounts for different consumption rates of different groups of worker bees by task (*e.g.*, nurse bees consume more pollen than other bees). Generally, this analysis considers that honey bee colonies consume an order of magnitude more nectar than pollen daily (Seely, 1985, clothianidin spiked sucrose and pollen patty CFS data in MRIDs 49836101 and 50312501, and derived Bee-REX food consumption rates). Comparison of colony-level toxicity data indicates that similar effects occur in colonies exposed to contaminated sucrose at lower concentrations compared to colonies exposed to residues in pollen (MRIDs 49836101 and 50312501; also comparisons with imidacloprid spiked sucrose and pollen CFS studies in MRID 49510001 and Dively, 2016, respectively). This appears to be a result of the total dose the colony received, rather than any inherent toxicity difference between nectar and pollen exposures.. Analysis of these two robust lines of evidence indicate that the difference in contribution of colony's dose from pollen is approximately 20x less than that of nectar. Therefore, for the Tier II analysis, exposure ($C_{total-t}$) to honey bee colonies will be assessed by applying concentration data for pollen ($C_{pollen-t}$) and nectar ($C_{nectar-t}$) to **Equation 1. Attachment 1** provides full account of considerations and the method for assessing combined nectar and pollen exposure to honey bee colonies.

$$\text{Equation 1.} \quad C_{total-t} = C_{nectar-t} + \frac{C_{pollen-t}}{20}$$

The method for assessing pollen and nectar exposure at the colony level differs from the one used (the "bee bread methodology" in the preliminary bee assessment (USEPA, 2017)). As opposed to considering pesticide exposure through nectar and pollen separately, this assessment combines both matrices for a total diet approach (at the colony level).

2.11.2 Considering other lines of evidence

The higher tiered analysis relies heavily upon the Tier II CFS and available residue data in pollen and nectar. Other lines of evidence are also available that are considered in the risk conclusion. Those lines of evidence include: other Tier II toxicity studies (*e.g.*, tunnel studies), Tier III studies and reported incidents involving bees.

2.11.3 Drawing risk conclusions

Colony level risk conclusions are based on the weight of the available evidence. In cases where residues are below the CFS endpoints (*i.e.*, NOAECs and LOAECs), and no other evidence is available to suggest that there are risk concerns, a “low risk” conclusion is made for honey bee colonies. If residue data are above colony level endpoints, then the strength of the evidence is characterized. This assessment employs three categories (strongest, moderate and weakest) to convey the strength associated with the weight of evidence for a crop with risk concerns for colony level effects from clothianidin or thiamethoxam.

The strongest evidence of risk is represented by cases where assumptions related to exposure and effects are not expected to have a major influence on risk conclusions and there are multiple lines of evidence indicating the potential for effects to honey bee colonies. A strong evidence of risk may be represented by a case where many measured residues for the crop of interest exceed both the colony level LOAEC and NOAEC for a relatively long duration (*e.g.*, several weeks); residues that are an order of magnitude above CFS endpoints (indicating that only a small fraction of the honey bee colony’s nectar and pollen need to be from treated fields); and the observation that multiple locations in the residue trials and/or multiple crops within the crop group yielded residues above CFS endpoints. In addition, incident reports of bee kills may provide additional lines of evidence for a strong evidence of risk conclusion.

Moderate evidence of risk is represented by cases where some lines of evidence indicate risk concerns; however, not all lines of evidence suggest risk, or there are some uncertainties associated with the data that can influence the risk conclusion. An example of moderate evidence of risk may be a case where only a small proportion of residues (from a small proportion of sites) exceed CFS endpoints for a short period of time (*e.g.*, days). In this case, there is some uncertainty whether effects will occur because residues from some sites do not exceed CFS endpoints and because the relatively short exposure duration may not be sufficient to elicit effects (*i.e.*, in the available CFS studies, after 3 and 6 weeks of constant exposure, effects were observed to colonies).

The weakest evidence of risk is represented by cases where there is evidence to suggest colony level effects; however, it is not well supported by measured residue data for the chemical of interest. For example, this may be the case when only a few residues are above the CFS NOAEC but not the LOAEC and those residues only exceed for a few days and sites. Another example may be when risk findings rely exclusively on residue data that are extrapolated (bridged) from other neonicotinoids or different crop groups where the influence of crop on the magnitude of the residue is highly uncertain (*e.g.*, bridging residue data derived from seed treatment applications to turmeric seed piece treatments).

1.

2.

3 Exposure Characterization

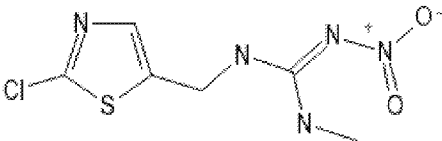
3.1 Physical, Chemical, Fate, and Transport Properties

3.1.1 Clothianidin

Clothianidin is very soluble (327 mg/L at 20°C) in water. The vapor pressure (3.8×10^{-11} mmHg) and Henry's Law Constant (2.9×10^{-11} atm m³/mol) indicate that the compound is non-volatile under field

conditions. For estimating exposures to bees via soil applications, it is necessary to use K_{oc} and K_{ow} as they influence the pesticide's mobility in water, corresponding to uptake within the plant following soil exposures. For estimating exposures to bees via soil applications, it is necessary to use K_{oc} and K_{ow} as they influence the pesticide's mobility in soil and water, corresponding to systemic uptake within the plant following root zone soil exposures. The values for clothianidin (*i.e.*, $\log K_{ow} = 0.64$, mean $K_{oc} = 160 \text{ L kg}_{oc}^{-1}$) used in this assessment are similar to those used thiamethoxam (*i.e.*, $\log K_{ow} = -0.13$, mean $K_{oc} = 70.2 \text{ L/kg}_{oc}$). The log octanol-water partition coefficient ($\log K_{ow} = 0.64$) for clothianidin indicates a low potential for bioaccumulation. Available data defining the physical, chemical, environmental fate and transport characteristics associated with clothianidin are summarized in **Table 3-1**.

Table 3-[SEQ Table * ARABIC \s 1]. Nature of the Chemical Stressor Clothianidin

Parameter	Value	Source/MRID #
Common name	Clothianidin	44703304
CAS number	210880-92-5 (previously 205510-53-8)	44703304
Chemical name (IUPAC)	(E)-1-(2-Chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine	44703304
Chemical Class	Neonicotinoid	44703304
Chemical Category	Insecticide	44703304
Empirical formula	$C_6H_8ClN_5O_2S$	44703304
Structure		44703304
Molecular mass	249.7 g/mole	44703304
Water solubility (20°C)	327 mg/L (at 20°C)	44703305
Vapor pressure (20 °C)	$3.8 \times 10^{-11} \text{ Pa}$ (at 20°C) ($2.9E-13 \text{ torr}$)	44703305
Henry's Law Constant	$2.9 \times 10^{-11} \text{ Pa} \times \text{m}^3/\text{mol}$ ($2.9E-16 \text{ atm} \cdot \text{m}^3/\text{mol}$)	Calculated ¹
Log octanol/water partition coefficient	0.64	EPISuite™ v4.11
Hydrolysis ($t_{1/2}$)	stable at pH 5 to 9 and 25°C	45422317
Direct Aqueous Photolysis ($t_{1/2}$)	14.4 hours (Phoenix, AZ summer sunlight)	45422318 45422319 45422320 45422321 45422322
Soil Photolysis	34 days (natural summer sunlight)	45422323
Aerobic Soil Metabolism ($t_{1/2}$)	148 – 1155 days (ten soils, all extrapolated first-order)	45422326 45422327 45422328
Aerobic Aquatic Metabolism ($t_{1/2}$)	177.7 days (total system, treated at 0.15 mg a.i./L) 182.4 days (total system, treated at 0.05 mg a.i./L)	46826903
Anaerobic Aquatic Metabolism ($t_{1/2}$)	27 days (total system)	45422330

Parameter	Value	Source/MRID #
Soil Partition Coefficient (K_{oc})	129 L kg _{o.c.} ⁻¹ for Quincy loamy sand 119 L kg _{o.c.} ⁻¹ for BBA 2.1 sand 123 L kg _{o.c.} ⁻¹ for Crosby clay loam 84 L kg _{o.c.} ⁻¹ for Laacher Hof sandy loam 345 L kg _{o.c.} ⁻¹ for Elder sandy loam	45422311
Time-dependent Soil Partition Coefficient (K_{oc}) ²	582 L kg _{o.c.} ⁻¹ (sandy loam soil 1.02% OC) 323 L kg _{o.c.} ⁻¹ (sandy loam soil 1.02% OC) 413 L kg _{o.c.} ⁻¹ (silt loam soil 0.83% OC) 311 L kg _{o.c.} ⁻¹ (silt loam soil 0.83% OC)	45422312
Terrestrial Field Dissipation ($t_{1/2}$)	Wisconsin (bare soil) 277 days North Dakota (bare soil) 1386 days Saskatchewan (bare soil) could not be determined as degradation was too slow Ohio (bare soil) 315 days Ontario (bare soil) 365 days California (bare soil) could not be calculated as degradation was too slow Washington (bare soil) 257 days Georgia (bare soil) 990 days Germany (lysimeter studies) no parent detected in leachate	45490703 45490704 45490705 45422331 45422332 45422333 45422334 45422335 45422336 45422508 45422604 45422612
¹ = Henry's Law (atm-m ³ /mole) = (VAPR/760)/(SOL/MWT), where VAPR is vapor pressure in torr, MWT is molecular weight in g/mol, and SOL is the solubility in water in mg/L. ² Reported values derived at study termination (99 days)		

In the environmental fate studies of clothianidin, several major degradates (>10% formation based on total radioactive residues) were observed in the aquatic photolysis study (including N-(2-chloro-5-thiazolyl-methyl)-N'-methylurea (TZMU) among others). TZMU was also observed at 10% in one of the terrestrial dissipation field study, and another major degradate, TMG, was observed in the aerobic aquatic metabolism study. However, most environmental fate studies did not report any major degradate formation. Minor degradate formation (<10%) was reported for the aerobic soil and aquatic metabolism studies (Table 3-2).

Table 3-[SEQ Table * ARABIC \s 1]. Major and Minor Degradates of Clothianidin^{1,2}

Fate Studies	Major Degradates (Max % of total dose)	Minor Degradates (Max% total dose)	Comments
Hydrolysis	None	None	No hydrolysis at 20°C
Aquatic Photolysis	MG = 34.7% (432 hrs); TZMU = 29.3- 39.7% (24 hrs); FA = 39.7% (24 hrs); HMIO = 26.6% (24 hrs); MU = 11.0% (432 hrs); MIT = 16.1% (120 hours)	None	None
Soil Photolysis	None	None	No degradates accumulated to

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			significant levels during the study.
Aerobic Soil Metabolism	None	MNG = 0.7 and 9.5% in Laacher Hof and Hofchen soils and 5.9% in BBA 2.2 soils; NTG = 3.7-6.7%; TZNG = 5.1-9.1% in the Laacher Hof, Hofchen, and BBA 2.2 soils and 2.5% in the Howe sandy loam soil; TZMU was 2.4% of the applied in all soils	Important route of degradation in clay loam soil.
Aerobic Aquatic Metabolism	TMG = 24.5% (91 days) and 13.8% (120 days)	TZMU = 1.4% (in total system and water), and at 0.8% the sediment	TMG was isolated almost entirely in the sediment as the maximum average concentration in the water was 0.6% of the applied.
Anaerobic Aquatic Metabolism	None isolated	None identified	Large amount of un- extracted residues
Terrestrial Field dissipation	TZMU = 10.1% at the Ohio test site	None identified	Degradation too slow in most sites for degradates to form.

¹ FA = formamide; HMIO = 4-hydroxy-2-methylamino-2-imidazolin-5-one; MG = methylguanidine; MIT = 7-methylamino-4H-imidazol[5,1-b][1,2,5]thiadiazin-4-one; MNG= N-methyl-N'-nitroguanidine; MU = methylurea; TMG = N-(2-chlorothiazol-5-ylmethyl)-N'-methylguanidine; TZMU = N-(2-chloro-5-thiazolyl- methyl)-N'-methylurea

² Degradate structures in **Appendix 1**

Degradation and Metabolism

Clothianidin appears to be a persistent compound under most field conditions. Based on analysis of the laboratory studies alone, the major route of dissipation for clothianidin would appear to be photolysis if exposure to sunlight occurs (*e.g.*, the measured aqueous photolysis half-life was <1 day; whereas, aerobic half-lives were 148 to 1155 days). Although photolysis appears to be much more rapid than other routes of degradation/dissipation of clothianidin in the laboratory studies, the slow rate of dissipation that was observed in field studies suggests that photolysis is not substantial under actual use conditions. Photolysis may be important in surface waters if residues have reached shallow, clear bodies of water. Clothianidin is stable to hydrolysis at environmental pH values and temperatures. Degradation under anaerobic aquatic conditions is quicker than aerobic soil metabolism.

Soil sorption and mobility

Clothianidin is mobile to highly mobile [MRID 45422311, soil organic carbon partition coefficient (Koc) values were 84 to 129 liters per kilogram organic carbon (L kg oc-1) for all laboratory test soils except for a sandy loam soil, which had a Koc value of 45 L kg o.c.-1], although only a modest amount of leaching was observed in the submitted field studies. The mobility of clothianidin appeared to decrease as the length of time clothianidin was in contact with the soil increased, *i.e.*, the longer clothianidin was aged in treated soil, the less likely it was to desorb from that soil. Sorption appeared to increase over time, as Koc values

[PAGE * MERGEFORMAT]

increased from 205 (low dose) and 153 (high dose) L kg o.c.-1 at Day 0 to 582 (low dose) and 323 (high dose) L kg o.c.-1 at Day 99 in the sandy loam soil. In the silt loam soil, Koc values increased from 120 (low dose) and 98 (high dose) L kg o.c.-1 at Day 0 to 413 (low dose) and 311 (high dose) L kg o.c.-1 at Day 99. It should be noted that at the end of the study, clothianidin comprised 56.3% and 58.0% of the applied radioactivity in the sandy loam and silt loam soils, respectively, and degradates were not identified. For this assessment, a mean Koc value of 160 L kg o.c.-1 was used in the exposure modeling.

Field dissipation

Clothianidin is expected to dissipate very slowly under terrestrial field conditions, based on the results of five bare ground field experiments conducted in the United States and Canada. Half-lives of clothianidin, based on residues in the 0-15 cm soil depth, were 277 days (Wisconsin sand soil, incorporated), 315 days (Ohio silt loam soil, not incorporated), 365 days (Ontario silt loam soil, incorporated), and 1,386 days (North Dakota clay loam soil, not incorporated), and could not be determined at a fifth site due to limited dissipation during the 25-month study (Saskatchewan silty clay loam soil, incorporated). Incorporation did not appear to be a significant factor in determining the rate of dissipation. Clothianidin was generally not detected below the 45 cm soil depth except at one site, where it moved into the 45-60 cm depth. No degradates were detected at >10% of the applied, and degradates were generally only detected in the 0-15 cm soil layer. This appears to agree with the time-dependent sorption study results presented above, where mobility decreased with time; however, those tests were only conducted for 99 days, while these studies were conducted for much longer periods of time. As with the time-dependent sorption study, in many of the field dissipation studies most of the parent remained untransformed at the close of the study; further accumulation of degradates could have occurred. It is uncertain if the substantial amount of clothianidin parent remaining in the soil profile at the close of these studies would leach if sufficient precipitation were to occur.

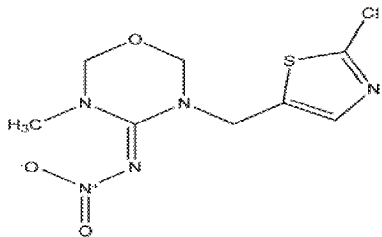
In residue monitoring studies, dissipation rates (DT50s) were calculated for the different measured matrices (pollen, nectar, leaves, and/or soil); DT50 values could not be calculated for all matrices due to a limited number of samples or the dissipation profile. These DT50 values for the different crops are discussed in the residue **Section 3.7**

3.1.2 Thiamethoxam

Thiamethoxam is very soluble (4100 mg/L at 25°C) in water. The vapor pressure (4.95×10^{-11} mm Hg) and Henry's Law Constant (4.63×10^{-15} atm m³/mol) indicate that the compound is non-volatile under field conditions. The log octanol-water partition coefficient (Log Kow = -0.13) for thiamethoxam indicates a low potential for bioaccumulation. Best-available data defining the physical, chemical, fate and transport characteristics associated with thiamethoxam are summarized in **Table 3-3**.

For estimating exposures to bees via soil applications, it is necessary to use Koc and Kow as they influence the pesticide's mobility in water, corresponding to uptake within the plant following soil exposures. For estimating exposures to bees via soil applications, it is necessary to use Koc and Kow as they influence the pesticide's mobility in soil and water, corresponding to systemic uptake within the plant following root zone soil exposures. The values for thiamethoxam (*i.e.*, log Kow = -0.13, mean Koc = 70.2 L/kg_{oc}) used in this assessment for thiamethoxam are similar to those used for clothianidin (*i.e.*, log Kow = 0.64, mean Koc = 160 L/kg_{oc}).

Table 3-[SEQ Table * ARABIC \s 1]. Nature of the Chemical Stressor Thiamethoxam

Parameter	Value	MRID
Common name	Thiamethoxam	44703304
CAS number	153719-23-4	44703304
Chemical name (IUPAC)	3-(2-Chloro-thiazolyl-5-ylmethyl)-5-methyl-[1,3,5]oxadiazinan-4-ylidene-N-nitroamine	44703304
Chemical Class	Neonicotinoid	44703304
Chemical Category	Insecticide	44703304
Empirical formula	C ₈ H ₁₀ ClN ₅ O ₃ S	44703304
Structure		44703304
Molecular mass (g/mol)	291.7	44703304
Water Solubility (25°C)	4100 mg/L	44703305
Vapor Pressure (25°C)	4.95 x 10 ⁻¹¹ mm Hg	44703305
Henry's Law Constant	4.63 x 10 ⁻¹⁵ atm m ³ /mol	Calculated ¹
Octanol/water partition coefficient (Log K _{ow})	-0.13 at 25°C	44703305
Hydrolysis (t _{1/2})	572 and 643 days at pH 7 (stable)	44703416
	4.2 and 8.4 days at pH 9	44703417
Direct Aqueous Photolysis (t _{1/2} ; d)	3.36	44715024
	3.90	44715025
Soil Photolysis (t _{1/2} ; d)	80	44715027
	97	44715028
Aerobic Soil Metabolism (t _{1/2} ; d)	294	44703419
	353	44703501
	101	44703418
	60.1	49589503
	174	49589504
	272	49589505
	188	49589506
	268	49589506
	464	49589506
	110	49589506
	136	49589506
	73.6	49589507
	143	49589507
Anaerobic Soil Metabolism (t _{1/2} ; d)	34.3	49589507
	81.3	49829901
	76.2	49829902
	77.7	49829902
	45.6	49829902
Aerobic Aquatic Metabolism (t _{1/2} ; d)	118	49829902
	16.3	44715032
	16.2	44715032
	35.1	49589509

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Parameter	Value	MRID
Anaerobic Aquatic Metabolism ($t_{1/2}$; d)	28.6	44715029
	25.3	44715030
	20.7	49589508
Soil Partition Coefficient (K_{oc} ; L/kg _{oc})	77.2 for Sandy Clay Loam	
	53.1 for Loam	44703502
	176.7 for Sandy Loam	44703503
	43.0 for Sand	45640401
	38.3 for Loam	45084901
	33.1 for Silty Clay Loam	
	[mean = 70.2 L kg_{oc}.⁻¹]	
Terrestrial Field Dissipation ($t_{1/2}$; d)	72-111 (seed treatment)	44703505
	13 (broadcast application)	44727506
	70.7 (broadcast application)	44948902
	100.4 (furrow application)	45086202
	1.05 to 78.8 (turf)	44948903
	56-133 (furrow + foliar)	50265301
Aquatic Field Dissipation ($t_{1/2}$; d)	11.6 to 17.2 (paddy water)	47558101
	13.6 to 26.7 (paddy soil)	47558102
		47558103
¹ = Henry's Law (atm-m ³ /mole) = (VAPR/760)/(SOL/MWT), where VAPR is vapor pressure in torr, MWT is molecular weight in g/mol, and SOL is the solubility in water in mg/L.		

Abiotic Degradation

Abiotic degradation of thiamethoxam is dominated by photodegradation in water with half-lives ranging from 3.4 to 3.9 days and alkaline-catalyzed hydrolysis (pH 9: 4.2-8.4 d). Thiamethoxam is hydrolytically stable in pH 5 and pH 7 buffered solutions. The main hydrolysis degradates are CGA-355190 and NOA-404617. The major photodegradation product in water is CGA-353042. Soil photolysis half-lives for thiamethoxam ranged from 80 to 97 days in irradiated soil. Several minor photodegradates in soil included CGA-355190, CGA-353968, CGA-322704, and CGA-282149. Major and minor degradates of thiamethoxam are listed in the **Table 3-4**. CGA-322704 is the chemical code for clothianidin.

Table 3-[SEQ Table * ARABIC \s 1]. Major and Minor Degradates of Thiamethoxam 1 Identified in

Laboratory and Field Studies

Table 3.4. Major and Minor Degradates of Thiamethoxam ¹ Identified in Laboratory and Field Studies

<i>Degradate</i>	<i>Hydrolysis</i>	<i>Photolysis (aqueous)</i>	<i>Photolysis (soil)</i>	<i>Aerobic Soil</i>	<i>Anaerobic Soil</i>	<i>Aerobic Aquatic</i>	<i>Anaerobic Aquatic</i>	<i>TFD</i>	<i>AFD</i>
CGA-265307	--	--	--	5.1	0.3	--	--	--	--
CGA-282149	--	--	3.17	6.8	--	--	--	--	--
CGA-309335	9.10	--	--	0.3	--	--	--	--	--
CGA-322704	--	--	2.44	36.8	17.3	--	< 3.8	13*	8.8
CGA-353042	--	60.7	--	--	--	--	--	--	10.2
CGA-353968	--	--	1.13	3.8	--	9.8	< 3.8	--	--
CGA-355190	59.5	--	2.22	23.7	21.5	78.9	31.3	30	10.0
NOA-404617	35.2	--	--	--	7.6	36.0	7.7	--	
NOA-407475	--	--	--	--	14.2	52.0	69.1	--	9.1
NOA-459602	--	--	--	--	4.0	--	--	--	--
SYN501406	--	--	--	--	2.6	--	--	--	--
UER	--	--	--	21.4	14.2	59.1	51.2	--	--
CO ₂	--	--	--	44.2	41.5	33.3	2.6	--	--

¹Maximum percent formation from all available fate studies. Percent formation varies by individual study.

*percentage estimated from soil concentrations which varies by soil type and depth.

CGA-322704 is the active ingredient clothianidin.

TFD = Terrestrial Field Dissipation; AFD = Aquatic Field Dissipation; UER = Unextracted Residues

Degradation and Metabolism

In terrestrial environments, thiamethoxam is expected to be persistent, with half-lives on the order of months to years. Thiamethoxam persists from months to years in various aerobic soils with (14) half-lives ranging from 34.3 to 464 days (90th percentile half-life = 236 days; half-life > 100 days in 11 of 14 studies) from (8) aerobic soil metabolism studies. Thiamethoxam persists for months with (5) anaerobic soil half-lives ranging from 45.6 to 118 days (90th percentile half-life = 97 days) from two anaerobic soil metabolism studies. Photodegradation in soil is not expected to be a substantial route of dissipation, as half-lives range from 80 to 97 days in irradiated soil.

Thiamethoxam is less persistent in aquatic environments, with half-lives on the order of weeks. In aerobic aquatic metabolism studies, thiamethoxam degraded with half-lives ranging from 16.2 to 35.1 days in water sediment systems. Thiamethoxam showed similar persistence in anaerobic aquatic environments with half-lives ranging 20.7 to 28.6 days. Unextracted residues accounted as much as 59% of total residues in aerobic aquatic metabolism studies.

Sorption and Mobility

Batch equilibrium studies indicate that thiamethoxam is mobile to moderately mobile in soils according to the FAO mobility classification (FAO, 2014). The adsorption K_{oc} values ranged from 33.1-176.7 L kg_{oc}⁻¹. Aged leaching studies also suggest that thiamethoxam becomes less mobile after aging.

Field Dissipation Studies

Several field dissipation studies were conducted in the United States and Canada (**Table 3.3**). Field dissipation half-lives for thiamethoxam varied depending on the type of application and crop treated. Dissipation half-lives ranged from 13 to 133 days. Thiamethoxam was detected at varying concentrations throughout the soil layers (0 - 90 cm soil depth). The major transformation products in the field studies were CGA-355190 (30% formation) and CGA-322704 (estimated 13% clothianidin formation).

Two aquatic dissipation studies of thiamethoxam under field conditions were conducted in Arkansas and Louisiana. These studies investigated the dissipation of thiamethoxam in a paddy water column and in soil when thiamethoxam was applied as a rice seed treatment. Aquatic field dissipation half-lives ranged from 11.6 to 17.2 days in paddy water to 13.6 to 26.7 days in soil. The major transformation products in paddy water were CGA-355190 (in Arkansas) and CGA-335190 and CGA-353042 (in Louisiana).

Aquatic and terrestrial field dissipation half-lives are similar to or within an order of magnitude of degradation half-lives conducted in the laboratory.

In the pollinator residue monitoring studies, dissipation rates (DT_{50s}) were calculated, when possible, for the different measured matrices (*i.e.* pollen and nectar). This analysis focused on pollen and nectar as the matrices relevant to bee exposure as well as other relevant surrogates (*i.e.* anthers, whole flowers). An analysis of concentrations in leaf tissue indicated that dissipation were dissimilar from these floral matrices. These DT₅₀ values for the different crops are discussed in the residue **Section 3.7**.

3.2 Plant Uptake

3.2.1 Clothianidin

A laboratory study to investigate the leaching of clothianidin in soil columns with corn (*Zea mays*) plants provides evidence for its systemic uptake in plants (MRID 47483002). Under the conditions tested, the route of dissipation for clothianidin was: (1) transfer from treated seeds to the surrounding surface soil (maximum of 76% of applied radioactivity); and, (2) uptake into root/plant tissue (residues in the plant increased during the duration of the study, reaching a maximum of 6.58% of the applied at 16 weeks). Leaching was minimal (cumulative 0.18% of applied at 16 weeks). Because of the long soil half-life demonstrated (165 days), and the minimal leaching, there is the potential for clothianidin to continue to be available for plant uptake, either in the crop to which it was applied, or to a subsequently planted crop. The maximum plant uptake of clothianidin in the study was expected to exceed the 6.58% demonstrated at the end of the experiment, as the plant residues were still rising and 70% of the applied clothianidin residues still remained in the surface soil at the end of the study.

3.2.2 Thiamethoxam

Several studies were conducted to understand the nature of thiamethoxam residues in various crop commodities after thiamethoxam application (MRIDs 44703511, -12, -15, -16, -20, and -21). These included foliar application to pears and cucumbers, soil applications to cucumbers and corn, seed treatments to corn and combination soil/foliar application to cucumbers. Radio-labeled studies were conducted with both [thiazol-2-¹⁴C] or [oxadiazin-4-¹⁴C] thiamethoxam. The studies indicate various application rates and methods result in thiamethoxam residues in plants suggesting uptake is possible. A brief summary of the results follows for each crop commodity. These summaries are not inclusive of all residues found in these studies but demonstrate differential uptake is possible in different plant parts based on application methods. For details see USEPA 2000 (HED Memo DP:252021)

In pears, foliar applications were made twice at nominal application rates of 0.23 or 2.29 lb c.e./A resulting in total radioactive residues (TRR) in/on fruit of 0.488 and 0.701 mg/kg (parts per million; ppm) for each radio label at the 0.23 lb c.e./A rate 15 days after the last treatment. The residues were an order of magnitude higher for the 2.29 lbs c.e./A rate, and two orders of magnitude higher in leaves for both rates. respectively with thiamethoxam and its clothianidin metabolite (CGA-322704) were the major components of the residue, accounting for 28-33% and 15-24% of the TRR, respectively.

In cucumbers, residues were analyzed in leaves and fruit following: 1) a soil drench was applied to seedlings at the first true-leaf stage at 1.14 lbs c.e./A followed 42 days later by a broadcast foliar application for a total of 1.52 lbs c.e./A, 2) a soil drench at 1.14 lbs c.e./A (with samples collected 42 d later) and 3) a foliar application of 0.08 lb c.e./A (with samples collected 14 d later). Following the combined soil and foliar application, residues in leaves were 9800-11700 ng c.g./g and 253-276 ng c.g./g in fruit. After the soil drench application, residues were similar to those of the combined foliar and soil application, with residues in leaves ranging 9440-14000 ng c.g./g and 240-328 ng c.e./g in fruit. Residues in leaves and fruit from the plants that only received a foliar spray were an order of magnitude lower than the other two application scenarios. Clothianidin was also detected in cucumber fruit as a minor degradate.

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In corn, residues were analyzed in leaves (forage) and grain following seed treatments of 1.03 mg a.i./seed. Residues in foliage at 14 days were at 63,000 ng c.e./g and declined at each subsequent sampling interval (at 33 d residues were 11,800 ng c.e./g; at 124 d, residues were 97 ng.c.e./g). Corn grains were sampled at 166/152 days (maturity), with residues of 13-20 ng c.e./g. Clothianidin was measured in leaves and grain at comparable levels as thiamethoxam.

3.3 Plant Metabolism

3.3.1 Clothianidin

Several plant metabolism studies for clothianidin are available including two corn studies reflecting application of [nitroimino-¹⁴C] clothianidin technical (TI-435) and [thiazolyl-¹⁴C] clothianidin technical as seed treatments (MRID 45422527 and 45422528), a sugar beet study reflecting application of [nitroimino-¹⁴C] clothianidin technical as a seed treatment (MRID 45422529), an apple study reflecting foliar application of [nitroimino-¹⁴C] clothianidin technical (MRID 45422532), and two tomato studies reflecting soil and foliar application of [nitroimino-¹⁴C] clothianidin technical (MRID 45422530 and 45422531). In the corn metabolism study reflecting thiazolyl labeling and in the metabolism studies reflecting nitroimino labeling, parent clothianidin was the predominant residue (26-95% of total radioactive residues depending on corn matrix and ring label), and the majority of the metabolites bore both the nitroimino and thiazolyl moieties. However, the identification of metabolite CTCA (chlorothiazolecarboxylic acid) in the metabolism study using thiazolyl labeling (corn seed treatment), and the identification of metabolites MNG (methylnitroguanidine), NTG (nitroguanidine), and MG (methylguanidine) in the metabolism studies using nitroimino labeling, confirm that cleavage of the clothianidin technical molecule occurs during plant metabolism (HED memo, D282446). The formation and quantity of the metabolites TMG, TZMU, MNG, NTG, and/or TZNG were minor and accounted for <10% of the residues. This general trend where clothianidin is the predominant residue was observed in the other metabolism studies as well (*i.e.*, sugarbeet, apple, tomato) with most metabolites <10% of the total radioactive residues

3.3.2 Thiamethoxam

Several metabolism studies involving applications of radiolabeled thiamethoxam are available to identify residues in plants. These studies indicate that, the oxadiazine ring of thiamethoxam is cleaved to form clothianidin, which is further metabolized over time. In the study involving lettuce (MRID 46093714), approximately 20 degradates were detected. This is consistent with other metabolism studies (*e.g.*, in corn following seed treatment 18 metabolites were detected; MRID 44703515). The magnitude of thiamethoxam and clothianidin residues in plant samples (leaves, fruit or tubers) varies by crop and time; however, clothianidin is often a major degradate (*i.e.*, >10% of total residues). In some studies, and time points, residues of thiamethoxam are greater, while in others, residues of clothianidin are equal or greater (**Table 3-5**).

Table 3-[SEQ Table * ARABIC \s 1]. Summary of thiamethoxam and clothianidin contents in plant metabolism studies involving thiamethoxam applications

Crop (matrix)	Application method	Days after last application	% radioactivity as Thiamethoxam	% radioactivity as Clothianidin	MRID
Pear (fruit)	Foliar	15	29	22	44703511
Lettuce (leaves)	Foliar	0	78-83	2.1	46093714
		3	66-70	3.2-3.2	

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Crop (matrix)	Application method	Days after last application	% radioactivity as Thiamethoxam	% radioactivity as Clothianidin	MRID
		7	63-55	3.5-3.8	
		14	38-42	5.6-5.8	
Cucurbits (fruit)	Foliar	14	11	1	44703512
Cucurbits (fruit)	Soil + foliar	14	13.5	3	44703512
Potatoes (tuber)	Seed treatment	84-106	12	6-13	45093713
Corn (leaves)	Seed treatment	78	4.3	12	44703515
Corn (leaves)	Seed treatment	166	7.9	9.8	44703520

3.4 Potential for Bee Exposure

The first step in this considering potential risk to bees involves a qualitative assessment of the potential for exposure of bees to clothianidin and thiamethoxam. This exposure potential is a function of the application rate and method, plant uptake and dissipation of the chemical, timing, location (*e.g.*, indoor vs. outdoor), the attractiveness of the crop to bees, agronomic practices (*e.g.*, timing of harvest), and the availability of alternative forage sources. For informing the potential for exposure of bees to clothianidin and thiamethoxam on the treated site, information on the attractiveness of crops is based on profiles developed by USDA (2015).

Figure 3-1 below summarizes the process for determining whether an on-field or off-field assessment is warranted. Consistent with the guidance, for soil and/or seed treatment uses, it is assumed that contact exposure on the treated field would be negligible, but oral exposure to residues in pollen and nectar may occur, provided the crop is attractive and is not harvested prior to bloom. As spray drift would not be present from these use patterns, there would be no off-field exposure expected.

Tables 3-6, 3-7, and 3-8 provide a summary of information on the bee attractiveness of crops with registered foliar, soil, and seed treatment uses of clothianidin and thiamethoxam, respectively. This table also indicates whether a Tier I contact and/or oral assessment is conducted for on-field and off-field based on crop attractiveness and cultural practices for each use (*i.e.*, whether the crop is harvested before the blooming period).

For any use with a foliar spray component, a Tier I off-field assessment is conducted for contact and oral exposure routes regardless of whether the crop is attractive or is harvested prior to bloom. This is due to the potential for bees to be exposed to spray drift while visiting fields adjacent to the treatment site. If the crop is attractive and is harvested after bloom, a Tier I on and off-field assessment is conducted for contact and oral exposure routes.

Where uncertainty exists about the crop's attractiveness to bees or harvest time (in relation to flowering), it is assumed that the crop will be attractive to bees and harvested after the bloom period, thereby necessitating on-field and off-field Tier I assessments for contact and oral exposure routes.

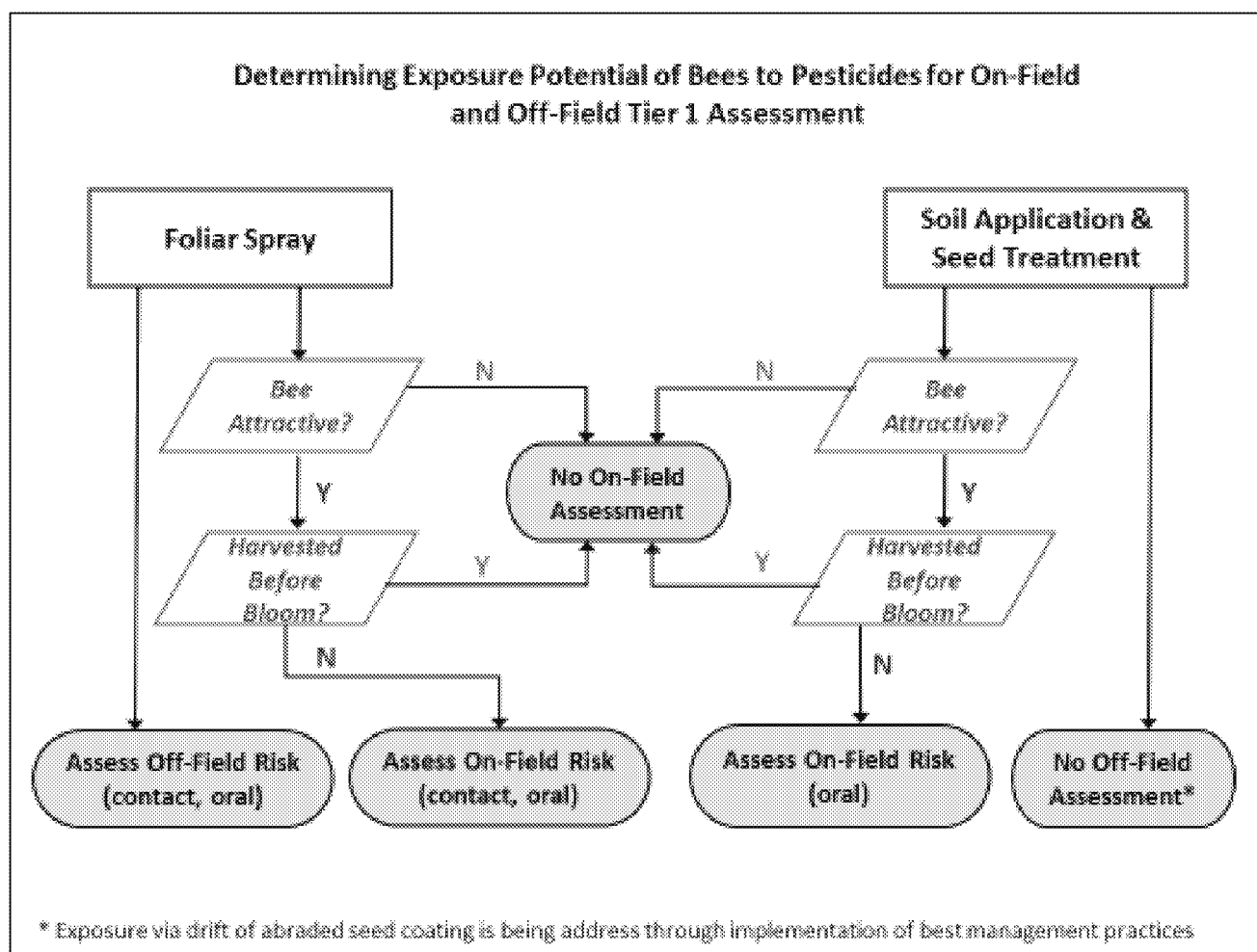


Figure 3-[SEQ Figure * ARABIC \s 1]. Summary of the potential scenarios warranting a Tier I on- and/or off-field pollinator risk assessment.

For the tables below, the attractiveness and harvesting information presented represents the most conservative scenario that would warrant Tier I on-field and off-field assessment. For example, if a certain member of a crop group indicates no attractiveness to bees, yet another crop within the group is considered attractive, a Tier I on-field and off-field assessment would be conducted.

Table 3-[SEQ Table * ARABIC \s 1]. Attractiveness of crops to bees for the registered foliar uses of clothianidin and thiamethoxam (as indicated by USDA, 2017)

Crop Group Number (Crop Group Name)	Honey Bee Attractive?	Bumble Bee Attractive?	Solitary Bee Attractive ?	Notes	Tier I On-Field Contact/Oral Assessment?	Tier I Off-Field Contact/Oral Assessment?
<i>Crop Group 1 – Root and Tuber Vegetables*</i>	Y (Pollen and Nectar)	Y	Y	Bees important for seed production, typically harvested prior to bloom. Potatoes noted to be harvested after bloom	Y	Y
<i>Crop Group 4 – Leafy Vegetables (Except brassica Vegetables)</i>	Y (Pollen and Nectar)	Y	Y	Bees important for seed production, typically harvested prior to bloom.	N	Y
<i>Crop Group 5 – Brassica (Cole) Leafy Vegetables</i>	Y (Pollen and Nectar)	Y	Y	Bees important for seed production, typically harvested prior to bloom.	N	Y
<i>Crop Group 6 - Legume Vegetables (Succulent or Dried)</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
<i>Crop Group 8 – Fruiting Vegetables (Except Cucurbits)*</i>	Y (pollen and nectar)	Y	Y	Some crops may be grown in glasshouses, with bumble bees for pollination	Y	Y
<i>Crop Group 9 – Cucurbit Vegetables*</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
<i>Crop Group 10 – Citrus Fruits</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
<i>Crop Group 11 – Pome Fruits*</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
<i>Crop Group 12 – Stone Fruits*</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
<i>Crop Group 13-07 – Berry and Small Fruit*³</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
<i>Crop Group 14 – Tree nuts</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
<i>Crop Group 15 – Cereal Grains</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
<i>Crop Group 19 – Herbs and Spices</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y

Crop Group Number (Crop Group Name)	Honey Bee Attractive?	Bumble Bee Attractive?	Solitary Bee Attractive ?	Notes	Tier I On-Field Contact/Oral Assessment?	Tier I Off-Field Contact/Oral Assessment?
<i>Crop Group 20 – Oilseed*</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
<i>Crop Group 23 – Tropical and Subtropical Fruit, Edible Peel Group</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
<i>Crop Group 24 – Tropical and Subtropical Fruit, Inedible Peel Group</i>	Y (Pollen and Nectar)	Y	Y	--	Y	Y
Non-crop group uses (artichoke, tobacco)	Y (Pollen and Nectar)	Y	Y	- tobacco deflowered as part of the harvest process artichoke harvested prior to bloom and requires pollination only for breeding	N	Y

Groups where members have residue data available are indicated with *

Table 3-[SEQ Table * ARABIC \s 1]. Attractiveness of crops to bees for the registered soil uses of clothianidin and thiamethoxam (as indicated by USDA, 2017)

Crop Group Number (Crop Group Name)	Honey Bee Attractive?	Bumble Bee Attractive?	Solitary Bee Attractive?	Notes	Tier I On-Field Oral Assessment?	Tier I Off-Field Contact/Oral Assessment?
<i>Crop Group 1 – Root and Tuber Vegetables*</i>	Y (Pollen and Nectar)	Y	Y	Bees important for seed production, typically harvested prior to bloom. Potatoes noted to be harvested after bloom	Y	N
<i>Crop Group 4. Leafy Vegetables (Except Brassica Vegetables)</i>	Y (Pollen and Nectar)	Y	Y	Bees important for seed production, typically harvested prior to bloom.	N	N
<i>Crop Subgroup 5-B. Brassica Leafy Greens Subgroup</i>	Y (Pollen and Nectar)	Y	Y	Bees important for seed production, typically harvested prior to bloom.	N	N
<i>Crop Group 8 – Fruiting Vegetables (Except Cucurbits)*</i>	Y (Pollen and Nectar)	Y	Y	Some crops may be grown in glasshouses, with bumble bees for pollination	Y	N
<i>Crop Group 9. Cucurbit Vegetables*</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 10. Citrus*</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 11. Pome Fruits</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 12. Stone Fruit</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 13-07 – Berry and Small Fruit²</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 14. Tree Nut</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 24 – Tropical and Subtropical Fruit, Inedible Peel Group</i>	Y (Pollen and Nectar) ⁺	Y ⁺	Y ⁺	--	Y	N
Non-crop group uses (artichoke, tobacco)	Y (Pollen and Nectar)	Y	Y	- tobacco deflowered as part of the harvest process; artichoke harvested prior to bloom and requires pollination only for breeding,	N (tobacco) Y for all others	N

Groups where members have residue data available are indicated with *

*Information was not available from USDA 2017 document; EPA assumes crops without USDA attractiveness data are attractive.

Table 3-[SEQ Table * ARABIC \s 1]. Attractiveness of crops to bees for the registered seed treatment uses of clothianidin and thiamethoxam (as indicated by USDA, 2017)

Crop Group Number (Crop Group Name)	Honey Bee Attractive?	Bumble Bee Attractive?	Solitary Bee Attractive?	Notes	Tier I On-Field Oral Assessment?	Tier I Off-Field Contact/Oral Assessment?
<i>Crop Group 1 – Root and Tuber Vegetables</i>	Y (Pollen and Nectar)	Y	Y	Bees important for seed production, typically harvested prior to bloom. Potatoes noted to be harvested after bloom	Y	N
<i>Crop Group 3 – Bulb Vegetables</i>	Y (Pollen and Nectar)	Y	Y	Bees important for seed production, typically harvested prior to bloom.	N	N
<i>Crop Group 4 – Leafy Vegetables (Except brassica Vegetables)</i>	Y (Pollen and Nectar)	Y	Y	Bees important for seed production, typically harvested prior to bloom.	N	N
<i>Crop Group 5 – Brassica (Cole) Leafy Vegetables</i>	Y (Pollen and Nectar)	Y	Y	Bees important for seed production, typically harvested prior to bloom.	N	N
<i>Crop Group 6- Legume vegetables *</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 9 - Cucurbit vegetables*</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 15 – Cereal Grains *</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 19 – Herbs and Spices</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 20 - Oilseed *</i>	Y (Pollen and Nectar)	Y	Y	--	Y	N
<i>Crop Group 18 – Non-grass Animal Feeds (Forage Fodder, Straw and Hay)</i>	Y (Pollen and Nectar)	Y	Y	Alfalfa grown for forage is harvested at 10% bloom, unless grown for seed,	Y	N
Non-crop group uses (peanut)	Y (Pollen and Nectar)	Y	Y	--	Y	N

Groups where members have residue data available are indicated with *

An additional consideration is the use of managed pollinators for crop production. For some crops, growers bring in managed bees to augment the pollination services of local bees if the crop requires pollination and wild bee populations are insufficient for adequate pollination. These commercially managed bees may include honey bees, bumble bees, mason bees, alfalfa leaf cutting bees, *etc.* When commercially managed bees are used to pollinate a crop, the potential for exposure and the magnitude of that exposure to the pollinating bees may be greatly increased. In order to reduce contact exposures to managed bees, clothianidin and thiamethoxam labels prohibit applications at bloom for crops with contracted pollination services.

3.5 Tier I (default) Exposure Estimation

As described above in **Section 2**, the pollinator risk assessment process is a tiered approach that begins with model-generated or default estimates of exposure and laboratory toxicity data at the individual bee level (Tier I). These estimates are also based on the bee's life stage (*i.e.*, adult vs larvae), consumption rates (of 0.292 g/day for adults and 0.124 g/day for larvae) of pollen and nectar, and the rate and method of application (*i.e.*, foliar, soil, or seed treatment applications).

For foliar applications, the Bee-REX model uses a standard contact dose rate of 2.7 µg a.i./bee per 1 lbs. a.i./A, while using a standard dose of 32 µg c.e./bee per 1 lb. a.i./A for adults and 13.6 µg c.e./bee for larvae based on consumption rates²¹ for these life stages to estimate dietary exposure. These standards are multiplied by the application rate to yield contact and oral doses for adults and larvae. For soil applications, the oral exposure estimates for adults and larvae are determined using Ryan-Briggs model estimates (based on application rate, log KOW [0.64] and organic carbon partition coefficient KOC of clothianidin [160]) multiplied by the adult and larval food consumption rates. The Tier I EECs for the range of application rates for clothianidin and thiamethoxam for foliar, soil, and seed applications are presented in **Tables 3-9- 3-12**.

Measured residue data are used to refine Tier I RQ values. The refined RQs and EECs for specific crop groups are discussed in **Section 5.2**.

Exposure Estimation - Foliar Uses

Table 3-[SEQ Table * ARABIC \s 1]. Tier I screening-level EECs for contact exposure to honey bees resulting from foliar uses of clothianidin and thiamethoxam (screening-level contact on-field)

Chemical	Assessed Appl. Rate (lbs c.e./A) ¹	Dose (µg c.e./bee) per 1 lbs. a.i./A)	Contact Dose (µg c.e./bee)
Thiamethoxam	0.04	2.7	0.11
Clothianidin and Thiamethoxam	0.08	2.7	0.22
Clothianidin and thiamethoxam	0.2 (0.23)	2.7	0.54 (0.62)
Clothianidin	0.4	2.7	1.1

¹The range of thiamethoxam application rates in terms of clothianidin equivalents is (0.04 - 0.08 lbs c.e./A with the upper-bound of non-agricultural uses at 0.23); The range of clothianidin application rates is (0.05 - 0.4 lbs c.e./A with the upper bound of non-agricultural uses at 0.4)

²¹ Tables summarizing the contact/dietary exposure estimates, and food consumption rates can be found in USEPA 2014b.

Table 3-[SEQ Table * ARABIC \s 1]. Summary of Tier I screening-level EECs for oral exposure to honey bees resulting from foliar uses of clothianidin and thiamethoxam (based on model-generated exposure values on-field).

Chemicals	Assessed Appl. Rate (lbs c.e./A) ¹	Bee Life Stage	Dose (μg c.e./bee per 1 lbs. a.i./A) ²	Oral Dose (μg c.e./bee)
Thiamethoxam	0.04	Adult	32	1.3
		Larval	13.6	0.54
Clothianidin and Thiamethoxam	0.08	Adult	32	2.6
		Larval	13.6	1.1
Clothianidin and Thiamethoxam	0.2 (0.23)	Adult	32	6.4 (7.4)
		Larval	13.6	2.7 (3.1)
Clothianidin	0.4	Adult	32	13
		Larval	13.6	5.4

¹The range of thiamethoxam application rates in terms of clothianidin equivalents is (0.04 - 0.08 lbs c.e./A with the upper bound of non-agricultural uses at 0.23); The range of clothianidin application rates is (0.05 - 0.2 lbs c.e./A with the upper bound of non-agricultural uses at 0.5)

Exposure Estimation – Soil treatments

Table 3-[SEQ Table * ARABIC \s 1]. Summary of Tier I screening-level EECs for oral exposure to honey bees resulting from soil uses of clothianidin and thiamethoxam (based on model-generated exposure values on-field).

Chemicals	Assessed Appl. Rate (lbs c.e./A) ¹	Bee Life Stage	Dose (μg c.e./bee per 1 lbs. a.i./A) ²	Clothianidin Oral Dose (μg c.e./bee)
Clothianidin and Thiamethoxam	0.09	Adult	0.05	0.002
		Larval	0.02	0.005
Clothianidin and Thiamethoxam	0.2 (0.23)	Adult	0.05	0.01 (0.01)
		Larval	0.02	0.004 (0.005)
Clothianidin	0.49	Adult	0.05	0.02
		Larval	0.02	0.01

¹ The range of thiamethoxam application rates in terms of clothianidin equivalents is (0.04 - 0.08 lbs c.e./A with the upper bound of non-agricultural uses at 0.23); The range of clothianidin application rates is (0.05 - 0.2 lbs c.e./A with the upper bound of non-agricultural uses at 0.49)

²Briggs EEC (derived from Bee-REX) * consumption rate for life stages (0.292g/day for adults; 0.124 g/day for brood)

Exposure Estimation – Seed treatments

For seed treatments, residues in pollen and nectar are estimated using concentrations in leaves and stems of treated plants. As described in the 2014 guidance document, the default value is assumed to be 1 microgram per gram ($\mu\text{g/g}$) or 1 ppm.

Table 3-[SEQ Table * ARABIC \s 1]. Summary of labeled use information for seed treatment applications of clothianidin and thiamethoxam (screening-level oral on-field)

Use pattern	Bee Life Stage	EEC in pollen and nectar	Oral Dose (μg c.e./bee/day)
	Adult		0.292

All registered seed	Larval	1 µg c.e./g (screening-level value for all seed)	0.124
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¹ Source: USEPA *et al.* 2014. Guidance for Assessing Pesticide Risks to Bees.

3.6 Refined Exposure Characterization

As described below, measured residues in pollen and nectar are available for clothianidin and thiamethoxam in certain treated crops. A summary of the residue concentrations for the Tier I refinement for clothianidin and thiamethoxam are presented below in **Table 3-13**. Additional details for each of the studies is described below in **Appendix 2** (clothianidin) and **Appendix 3** (thiamethoxam). When measured residues are available, these residue concentrations in nectar and/or pollen are combined with consumption rates (from BeeREX) to refine estimates of exposure to individual bees. These refined exposure values are then used to generate RQs which represents a refinement to the Tier I risk assessment (using measured residue values over modeled values). The maximum measured residue concentration is used to generate the acute RQs and the maximum mean residue concentration is used for chronic RQs.

Table 3-[SEQ Table * ARABIC \s 1]. Summary of the maximum single value and maximum mean residue concentration in pollen and/or nectar from the residue studies for clothianidin and thiamethoxam

Application Method	Crop	Clothianidin (ng/g)			
		Max concentration in pollen	Max concentration in nectar	Max mean concentration in pollen	Max mean concentration in nectar
Foliar	Potato (49705902)	119	--	76.1	--
	Pumpkin (49602802)	123	6.51	108	4.86
	Cotton (49904901)	4383	3364	1216	911
	Peach (50154303) [§]	130	< 1.0	49.7	< 1.0
	Apple (50154304)	57.4	< 1.0	31.2	< 1.0
	Grapes, post-bloom (50154305)	31.9	--	18.1	--
	Grapes, pre-bloom (50154305)	1564	--	1306	--
	Almond (50154302)	20.0	2.04	13.4	1.23
Soil	Potato (49705902)	188	--	92.5	--
	Pumpkin [pre-emergence] (49910601)	41.3	5.84	22.2	4.98
	Pumpkin [post-emergence] (49910601)	34.5	11.3	28	9.55
	Pumpkin [from 4 cucurbit study] (49705901)	40.2	7.28	16.9	5.39
	Cucumber (49705901)	--	39.7	---	32.6

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	Melon (49705901)	--	14.7	--	10.8
	Squash (49705901)	14.8	4.51	12	4.46
	Orange (49317901)	--	18.7	--	8.2
	Corn (49372102)	27.9	--	26.6	--
	Citrus (49944702)	--	15.0	--	< 2.5
	Popcorn (50009301)	129	--	60	--
	Grapes (50154305)	206	--	160	--
	Melon, bee-collected (50154306)	32.5	11.5	25.4	7.19
	Melon, hand-collected (50154306)	39.5	65.5	39.5 ^h	65.5 ^h
	Citrus (50478201)	631	114	412	64.6
Seed	Corn (scaled) ^e (49754402)	59.5	--	12.3	--
	Corn (unscaled) ^e (49754402)	23.8	--	4.91	--
	Canola (49754401)	4.14	1.84	2.79	1.44
	Cotton (49904901)	4.57	3.84	2.35	1.97
	Popcorn (50009301) ^f	14.2	--	7.5	--
	Corn (50154301) ^f	6.15	--	4.86	--
	Corn (50154301)	7.78	--	4.38	--
	Soybean (50025901)	< 0.3	< 0.3	< 0.3	< 0.3
	Soybean (50025902)	< 0.3	< 0.3	< 0.3	< 0.3
Thiamethoxam (c.e.)					
Application Method	Crop (MRID)	Max TR conc. in pollen	Max TR conc. in nectar (EFN conc.)	Max mean TR conc. in pollen	Max mean TR conc. in nectar (EFN conc.)
Foliar	Tomato (49804101)	14504	--	8909	--
	Cucumber (49804105)	1228	297	1049	168
	Cranberry (49804102)	1932	2107	1186	1057

	Stone Fruit (49819501)	328	5.49	160	2.48
	Cotton (49686801)	316	9.83 (675)	54.76	3.06 (80.84)
	Strawberry (50265502)	6463	567	5799	334
	Soybean (50265503)	545 ^b	44.3	486 ^b	42.5
	Apple (50265504)	2124	660	1756	496
	Pumpkin (50265506)	80.4	26.6	30.7	23.8
	Blueberry (50425901)	868	647	810	593
	Citrus (50425902)	878	12.1	703	10.0
	Ornamentals (50425903)	3127	1192	1238	796
Soil	Cucumber (49550801)	10.02	11.84	6.98	9.50
	Pepper (49804103)	268	1384	238	534
	FL Citrus (49881002)	323 ^a	23.71 ^a	69.47 ^a	12.80 ^a
	CA Citrus (49881001)	410 ^a	65.22 ^a	107 ^a	19.78 ^a
	Strawberry (50266001)	1669	186	1126	86.9
	Cucurbit (50265501)	755	57.6	310	28.7
	Tomato (50265507)	306	330 ⁱ	220	261 ⁱ
Seed	Soybean (49804104)	6.08 ^b	5.15	4.14 ^b	2.91
	Soybean (49210901)	23.14 ^c	--	15.64 ^c	--
	Canola (49819502)	46.89 ^d	13.34	46.89 ^d	8.08
	Canola (49755702)	7.69	2.64	3.17	1.48
	Cotton (49686801)	1.0	1.54 (1.74)	1.0	1.18 (1.25)
	Corn (49158916)	12.47	--	6.45	--
	Corn (49158914)	7.98	--	5.02	--
	Corn (49158915)	5.19	--	3.33	--
Seed + Foliar	Corn (50265505)	864	--	604	--

TR = Total Residue

EFN = extra floral nectar concentrations, where available (cotton).

^a = concentrations normalized to typical citrus application rate of 0.172 lb a.i./acre.

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^b = no pollen data. Whole flower and anther data available. Highest values presented from whole flower data.

^c = no pollen or nectar data. Values represent reproductive organ structure (stamen, pistil, nectary) data.

^d = highest clothianidin value (759 ppb) excluded. Next highest value (47 ppb) presented. Max and mean value are identical because there was only a single sampling interval.

^e = for this use, the “scaled” residue values are empirically measured residue concentrations which were adjusted upwards 2.5X to account for the maximum allowable rate for corn seed treatment. The “unscaled” values are the empirically measured residue concentrations before adjusting.

^f = this application consisted of treated seed plus an in-furrow application

^g = values for pollen could include a potential outlier. Replicate residues registered 9.16, 130, and 9.96 ng/g.

^h = mean and max concentrations are the same, as there was only one sample.

ⁱ = no nectar collected. Whole flower data

Use of Empirical Nectar and Pollen Residues for Tier II refinements

In the Tier II assessment, the maximum mean-measured²² residues in nectar and pollen are compared to endpoints from colony-level studies (six-week chronic exposure) where endpoints are expressed in terms of the concentration in spiked sucrose solution diet. Since honey bee colonies consume a combination of nectar and pollen, pesticide exposure can be assessed by considering both matrices. In order to assess exposure from total food, this method considers both the amount of each matrix consumed on a daily basis, as well as potential differences in toxicity to the colony that may be the result of different matrices. As discussed in detail in **Attachment 1**, this “total food” method is a weight-of-evidence approach based on colony biology and comparisons of available colony level toxicity studies from sucrose and pollen patties.

3.7 Additional Residue Information

Additional available residue information available for clothianidin and thiamethoxam include monitoring studies evaluating neonicotinoid residues in bee hives and crop rotational studies examining the carry-over of clothianidin and/or thiamethoxam residues in soil. These studies were determined to have limited utility for evaluating potential risks to bees posed by the use of clothianidin or thiamethoxam on treated crops. A discussion of their conduct and results is provided in **Appendices 2-3** for clothianidin and thiamethoxam, respectively.

²² Most acceptable residues studies have at least 3 sampling times per geographic site with each sampling point consisting of at least 3 replicate samples. The maximum mean-measured residue in a study is the highest average residue from a single sampling point in one site.

4 Effects Characterization

Over a hundred unpublished bee toxicity studies were submitted for clothianidin and thiamethoxam. Many additional studies have been published in the literature by various authors. Available studies included Tier 1 (laboratory) tests involving TGA1 or formulated products. Tier I studies are available for honey bees, bumble bees and other species of bees (referred to as “non-Apis”). Tier II (semi-field) studies are also available for honey bees, bumble bees and other species. These studies included a wide variety of study designs and approaches for testing the toxicity of clothianidin or thiamethoxam to honey bee or bumble bee colonies under somewhat controlled conditions. There are a limited number of valid Tier III (full field studies) available for either chemical. All of the available Tier III studies are limited in their reliability and are only considered useful for characterization purposes. This section summarizes the available Tier I, II and III toxicity data for clothianidin and thiamethoxam, with a focus on the most robust and reliable studies. Appendices 3 and 4 provide more details on the registrant submitted and published studies describing the toxicity of clothianidin and thiamethoxam (respectively) to bees. Available studies submitted by registrants or in the literature that are considered invalid are listed in **Appendix 4**.

4.1 Tier I

At the Tier I level, effects to individual bees are considered. Individual level toxicity endpoints (LD50 and NOAELs) are quantified using a suite of laboratory studies that assess effects to different life stages (*i.e.*, adults and larvae) and different durations of exposure, *i.e.*, acute (single dose) and chronic (repeat dose). The most sensitive apical (including survival, growth or reproduction) endpoints from the Tier I studies, from which findings can be statistically verified, are used to derive the Tier I default and Tier I refined RQs. Standardized test guidelines are available for Tier I studies (by EPA or OECD) and these are generally adhered to by the registrant-submitted studies. While test methods originating from the open literature can be more varied, the adult acute contact and adult acute oral tests evaluated from the open literature for clothianidin and thiamethoxam were also generally conducted in accordance with one or more published guidelines. This section summarizes the available Tier I toxicity data for honey bees and other species of bees from both registrant submissions and the scientific literature.

Table 4-1 below summarizes the most sensitive endpoints from each of the Tier I study types with further discussion of the studies provided in **Appendices 3** and **4**. Endpoints in this table originate from registrant- submitted studies conducted with *A. mellifera* as they provided raw data enabling independent verification of study results. This assessment uses the Tier I endpoints quantitatively for risk estimation for both clothianidin and thiamethoxam exposures. The most sensitive of either thiamethoxam or clothianidin values is used for both, based on the following rationale: a) the acute oral and acute contact toxicity values for these compounds are very similar; and b) clothianidin and thiamethoxam residues are considered jointly in the risk assessment where thiamethoxam exposures are expressed in terms of clothianidin equivalents.

Table [STYLeref 1 \s]-[SEQ Table * ARABIC \s 1]. Summary of most sensitive acute and chronic quantitative endpoints for honey bees exposed to clothianidin and thiamethoxam (expressed as clothianidin equivalents, c.e.). Bold values are those used to generate RQs for both chemicals. Values expressed on a dose (ug c.e./bee/day) basis.

Study Type	Measurement Endpoint	Value		MRID (Classification)	
		Clothianidin	Thiamethoxam	Clothianidin	Thiamethoxam

Adult Acute Contact Toxicity	96-hr LD ₅₀	0.0275	0.021	49950102 (Acceptable)	44714927 (Acceptable)
Adult Acute Oral Toxicity	48-hr LD ₅₀	0.0037	0.0038	45422426 (Acceptable)	49005702 (Acceptable)
Adult Chronic Oral Toxicity	10-day NOAEL	0.00036	0.0025	48414901 (Acceptable)	50084901 (Acceptable)
	10-day LOAEL	0.00072 (12% mortality)	0.0049 (70% mortality)		
Larval Acute (single dose)	LD ₅₀	NA	>0.03	NA	50096607 (Acceptable)
Larval Chronic (repeat dose)	21- day NOAEL	NA	0.0037	NA	50096607 (Acceptable)
	21- day LOAEL	NA	0.0066 (21% decrease in adult emergence)		

NA = not available

When considering the available acute toxicity data for honey bees exposed to clothianidin, adults are more sensitive on an oral exposure basis compared to contact exposure. Registrant submitted 48-h oral LD₅₀s range 0.0037-0.016 ug c.e./bee for TGA1, while contact-based 48-h LD₅₀s range 0.028-0.044 ug c.e./bee for TGA1. Qualitative acute toxicity data published in the literature are in general agreement with these endpoints. Available data for adult bumble bees suggest that honey bees and bumble bees are of similar sensitivity on a contact and oral basis. Acute toxicity data for larvae are not available for comparison to adults. On a chronic exposure basis, the NOAEL for adults is an order of magnitude below the most sensitive LD₅₀. When considering LOAEC values (based on mortality) for adults (17.7 ng c.e./g) and larvae (1500 ng c.e./g), adult bees are an order of magnitude more sensitive than larvae. When considering other test species, there is one chronic study available for alfalfa leaf cutter bees that suggest that their larvae are more sensitive to clothianidin than honey bee larvae.

Thiamethoxam toxicity data have a similar pattern, where for acute exposure to adults, the oral route (48-h LD₅₀s range 0.0038-0.0096 ug c.e./bee) is more sensitive than contact exposure (LD₅₀ = 0.021 – 0.11 ug c.e./bee). The available data suggest that bumble bee adults may be less sensitive to thiamethoxam compared to honey bees whereas stingless bees may be more sensitive. Although definitive LD₅₀ values were not established for honey bee larvae, the available information indicate that larvae are at least an order of magnitude less sensitive than adults. On a chronic exposure basis, adults are also more sensitive than larvae, with LOAEC values based on mortality of 0.0049 and 0.066 ug c.e./bee for adults and larvae respectively. When comparing the available toxicity data for honey bees, the acute adult endpoints overlap for clothianidin and thiamethoxam. The adult chronic endpoints are within a factor of 6 of each other, suggesting that the chronic toxicity of these chemicals to adults is similar. Larval toxicity data for clothianidin and thiamethoxam are in different units, which prevents comparison of toxicity to this life stage.

Figures 4-1 and 4-2 compare the acute oral and contact LD₅₀ values for *Apis* and non-*Apis* species exposed to TGA1 clothianidin or thiamethoxam. When comparing toxicity data for thiamethoxam and clothianidin for honey bees, these data indicate that the chemicals have similar toxicities. When adjusted for body weight on an individual basis, it appears that some non-*Apis* species (*i.e.*, bumble bee) may be less sensitive than honey bees on a contact exposure basis but more sensitive based on oral exposure. However, there are uncertainties in non-*Apis* food consumption rates and body weights which reduce the

certainty of these comparisons on a per body weight basis. In generally, non-Apis species are generally within a factor of 10x of honey bee acute toxicity endpoints.

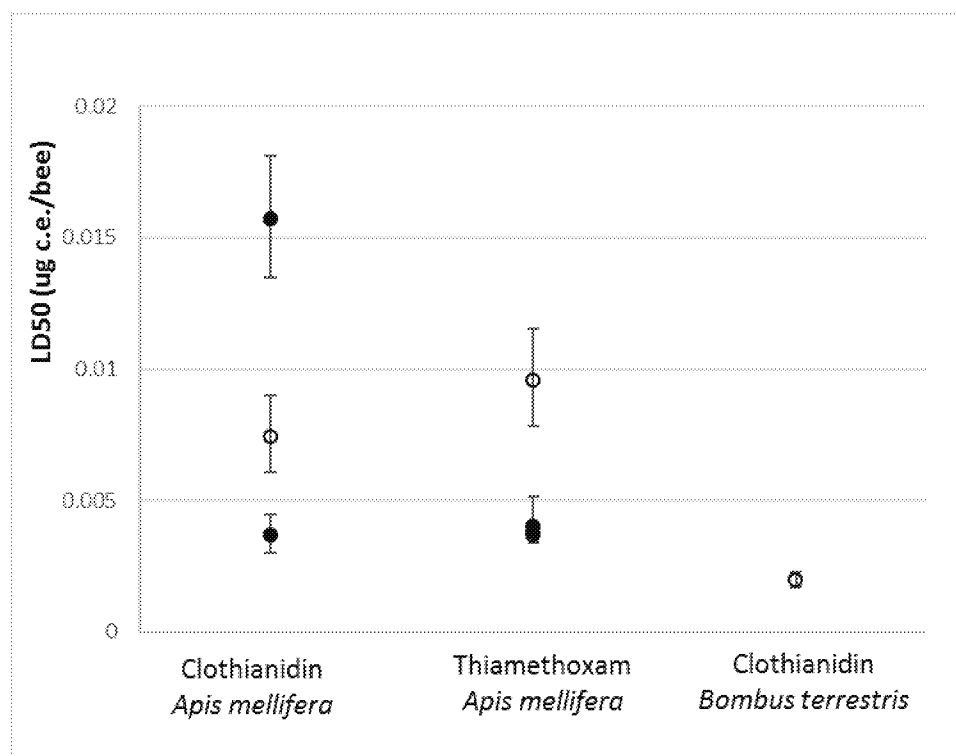


Figure 4-[SEQ Figure * ARABIC \s 1]. Adult LD50 values for oral exposures to TGAi thiamethoxam or clothianidin. Closed circles represent quantitative endpoints. Open circles represent qualitative endpoints.

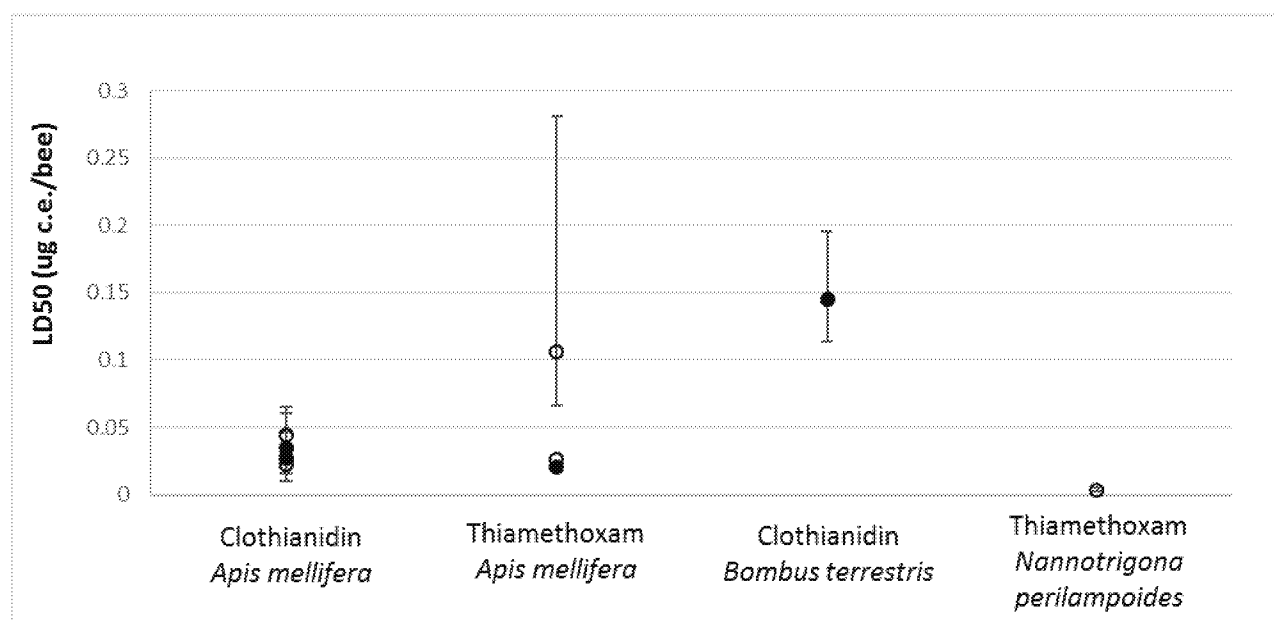


Figure 4-2. Adult LD50 values for contact-based exposures to TGAi thiamethoxam or clothianidin. Closed circles represent quantitative endpoints. Open circles represent qualitative endpoints.

4.2 Tier II

As discussed in the Pollinator Risk Assessment Guidance (USEPA *et al.* 2014), Tier II encompasses studies that characterize effects at the colony level. For honey bees, these studies are represented by different designs. There are two primary types of Tier II honey bee studies available for neonicotinoids: colony feeding and tunnel. The colony feeding study design involves exposure of whole colonies to pesticide-treated sucrose or pollen. In these studies, the colonies are not confined to enclosures (*i.e.*, the bees are free-foraging). The objective of these studies is to establish a no observed adverse effect concentration and a lowest observed adverse effect concentration for exposed colonies. Tunnel study designs generally involve exposure of small (nucleus) colonies to the pesticide of interest following application of the pesticide to a bee-attractive crop (*e.g.*, phacelia). Tier II studies are usually conducted under conditions that represent the worst-case exposure scenario (*e.g.*, highest registered application rate) for the colony whether in a tunnel environment or exposure through spiked diet. Tier II study designs may be amenable to additional treatment levels and replication, thus facilitating quantification of an application rate-response (semi-field tunnel study) or dose-response (feeding study) relationship at the colony level and determination of a NOAEC. For clothianidin and thiamethoxam, several registrant-submitted Tier II studies are available employing feeding study and tunnel study designs. Of the available studies, the most robust and reliable are the registrant-submitted colony feeding studies (CFS; with sucrose). This section summarizes the available honey bee, bumble bee and mason bee Tier II studies for clothianidin and thiamethoxam.

Honey bee colony feeding studies: sucrose exposure

Two sucrose CFS were submitted for clothianidin and two for thiamethoxam. For each chemical, one CFS was conducted in 2014 in a similar area in North Carolina. Both of these studies were considered scientifically valid but classified supplemental because they failed to adequately evaluate potential effects to exposed hives after overwintering (survival of control hives was low). As a result, sucrose-based CFSs were repeated for both clothianidin and thiamethoxam in 2016. Both studies were conducted in a similar area as the original studies (*i.e.*, NC). The second set of studies were carried out through the following spring, with an adequate overwintering period. When considering the four studies, effects were generally similar among the studies, with pronounced effects to the number of adults, eggs, larvae and pupae. No studies showed impacts to the amount of stored honey. Also, the second set of studies (conducted in 2016) did not show effects after overwintering. For clothianidin, the NOAECs from the two studies were 19 and 37 ng c.e./g, with corresponding LOAECs of 35.6 and 75 ng c.e./g. The endpoints from the two thiamethoxam studies were similar, with NOAECs of 25.3 and 43.6 ng c.e./g, with LOAECs ranging 34-81.6 ng c.e./g. **Table 4-2** summarizes the four registrant-submitted, sucrose-based CFSs for clothianidin and thiamethoxam, including the maximum decrease in each endpoint relative to the control. Appendices 3 and 4 include additional details on these four studies. When considering the effects observed in the 2014 sucrose CFSs compared to those conducted in 2016, the endpoints for the same chemical are within a factor of 2. Similarly, when comparing the clothianidin and the thiamethoxam endpoints from the same year, the endpoints are less than a factor of 2 apart. This suggests that the toxicities of clothianidin and thiamethoxam to honey bee colonies are similar. The endpoints from the most sensitive of the clothianidin CFS (MRID 49836101) are used to evaluate colony level effects of both chemicals. For thiamethoxam, endpoints from the study conducted in 2016 (MRID 50432101) are used as an additional line of evidence in

evaluating effects of thiamethoxam to honey bee colonies. The 2014 study is not used quantitatively in the Tier II risk assessment because of limitations of the study.

Table 4-2. Summary of registrant-submitted Tier II honey bee colony feeding studies involving sucrose exposure.

Test material	NOAEC (ng c.e./g)	LOAEC (ng c.e./g)	Effects observed at LOAEC (max % reduction compared to control at any CCA)						Year conducted	MRID (classification)
			Adults	Eggs	Larvae	Pupae	Pollen cells	Honey cells		
Clothianidin	19	35.6	30	22	NS	41	65	NS	2014	49836101 (supplemental)
	37	75	64	55	61	76	88	NS	2016	50312501 (acceptable)
Thiamethoxam	25.3*	34* (63)	25 (57)	13 (56)	35 (60)	42 (92)	42 (81)	NS	2014	49757201 ** (supplemental)
	43.6	81.6	NS	NS	51	46	80	NS	2016	50432101 (acceptable)

NS = not significantly different than control at the LOAEC

*There is uncertainty in whether the NOAEC is conservative. Due to this uncertainty, the two highest test levels where conservative effects were observed was used to characterize effects levels.

**Not considered suitable for quantitative use.

Table 4-3 includes a comparison of the Tier I and II endpoints for honey bees, with all effect values expressed on a concentration basis. When considering the four colony level studies, decreased number of adults were observed in the range of 34-75 ng c.e./g. This is consistent (*i.e.*, within a factor of 4) with the clothianidin chronic adult toxicity study where significant (12%) mortality was observed at 17.7 ng c.e./g. The thiamethoxam chronic adult toxicity study reported significant (70%) mortality at 181 ng c.e./g, which within a factor of 5 of the colony level endpoints; although it is less conservative. Effects to stored pollen, and brood (eggs, larvae and pupae) were also observed at 34-75 ng c.e./g. A decline in brood (eggs, larvae and pupae) were all observed at the same time points (CCAs) as adult declines. The Tier I toxicity data for larvae exposed to thiamethoxam (LOAEC = 200 ng c.e./g) suggests that there could be direct effects to larvae; however, this may not be the case based on the clothianidin study (LOAEC = 1500 ng c.e./g). Taken together, these studies suggest that direct toxicity to brood may not be the cause of observed effects in the colony studies. Decreased number of adult worker bees can lead to insufficient number of nurse bees to tend brood and forage for pollen. Hives stressed due to insufficient number of adult workers and food have been observed with increased brood loss (Winston 1987). Since the hives were fed sucrose, it is not surprising that the amount of stored honey is not significantly impacted.

Table [STYLEREf 1 \s]-3. Summary of most sensitive acute and chronic quantitative endpoints for honey bees exposed to clothianidin and thiamethoxam (expressed as clothianidin equivalents, c.e.). Values expressed on a concentration basis (ng c.e./g) to allow for comparison of clothianidin and thiamethoxam toxicity and to allow comparison of Tier I and II endpoints.

Endpoint	Chemical	Value	MRID	Comments
Adult Chronic Oral LOAEC (10 d)	Clothianidin	17.7	48414901	NOAEC = 9.1; 12% mortality observed at LOAEC
Colony level LOAEC (6-wk)	Thiamethoxam	34-63	49757201	NOAEC ~25.3; value is qualitative
Colony level LOAEC (6-wk)	Clothianidin	35.6	49836101	NOAEC = 19
Colony level LOAEC (6-wk)	Clothianidin	75	50312501	NOAEC = 37
Colony level LOAEC (6-wk)	Thiamethoxam	81.6	50432101	NOAEC = 43.6
Adult Chronic Oral LOAEC (10 d)	Thiamethoxam	181	50084901	NOAEC = 103; 70% mortality observed at LOAEC
Adult Acute Oral LC ₅₀	Thiamethoxam	~190	49005702	
Larval Chronic LOAEC (21-d)	Thiamethoxam	200	50096607	NOAEC = 112; 21% decrease in emergence observed at LOAEC
Adult Acute Oral LC ₅₀	Clothianidin	~420	45422426	
Larval Chronic LOAEC (21-d)	Clothianidin	1500	48448803	NOAEC = 680; 27% mortality observed at LOAEC
Larval Acute LC ₅₀	Clothianidin	>15000	48876801	
Larval Acute LC ₅₀	Thiamethoxam	>3110	50096607	

Honey bee colony feeding studies: pollen exposure

One pollen-based honey bee CFS has been identified for clothianidin. In addition, two pollen CFSs are available where bees were exposed to a combination of clothianidin and thiamethoxam.

The clothianidin pollen CFS was a pilot study conducted by the registrant (MRID 50478501). This study is considered scientifically valid and classified supplemental (details in **Appendix 5**). For hives exposed to 1460 ng c.e./g (pollen paddy), significantly lower number of adults, larvae, pupae and

stored food were observed relative to controls. The resulting NOAEC is 372 ng a.i./g. This study is used in the weight of evidence for establishing a weighting factor for adjusting concentrations of neonicotinoids in pollen to nectar equivalents. The nectar-equivalent concentrations are added to concentrations in nectar to estimate the total food exposure of a honey bee colony. Details of this approach are provided in **Attachment 1**.

A qualitative pollen CFS with full sized honey bees exposed to a combination of clothianidin and thiamethoxam are available in the literature. Sandroock et al. (2014b) observed effects to the number of adults, brood and stored honey and increases in queen effects (supersedure and swarming) in hives exposed to 6.6 ng c.e./g. This study is limited in design, with the major limitation being a lack of multiple test concentrations, preventing establishment of a NOAEC as well as low N. When the concentration-based test levels observed in Sandroock et al. are converted to a dose basis and compared to the dose-based effects level (*i.e.*, LOAEL) of the registrant-submitted study discussed in the previous paragraph, the values are within an order of magnitude. Given the limitations of this study, it is considered less reliable than the registrant-submitted pollen CFS.

An additional study involving exposures of nuclear colonies exposed to a combination of clothianidin and thiamethoxam is available; however, this study is also considered qualitative due to low replication (N = 3) and inclusion of only test level. Williams et al. (2015) observed effects to colonies exposed to 4.5 ng c.e./g, expressed as impacts to queens (decreased eggs laid, decreased number of worker offspring). Given the limitations of this study, it is considered less reliable than the registrant-submitted pollen CFS.

Bumble bee colony feeding studies

Several bumble bee CFSs are available for bumble bees (*Bombus terrestris* or *B. impatiens*) exposed to clothianidin and thiamethoxam. These studies are considered qualitative due to design limitations. They are considered useful in comparing the toxicity of clothianidin and thiamethoxam to honey bees and bumble bees.

Fausser-Misslin *et al.* 2014, fed *B. terrestris* with pollen and sugar water that were treated with both clothianidin and thiamethoxam (4.94 ng c.e./g clothianidin equivalents) for 9 weeks. Significant decreases in number of workers produced, worker longevity, food collection, and queen survival were reported. Elston et al. 2013 (MRID 49579002) examined the effects on nest building or brood production from dietary exposure of thiamethoxam in *B. terrestris* microcolonies. Bees were exposed for 28 days to thiamethoxam in honey water and pollen paste. At the 10 ng/g treatment, nest building initiation was delayed, fewer eggs were laid, and no larvae were produced. No effects were observed at 1 ng c.e./g. Stanley et al. 2015 investigated how exposure to thiamethoxam could affect the ability of bumblebees to pollinate apple trees. The study authors reported that in the 10 ng/g treatment there were lower visitation rates to flowers and lower numbers of bees carrying pollen. No effects were observed at 2.4 ng/g. In a study with *Bombus impatiens* (Scholer and Krischik 2014), colonies contained in a greenhouse were fed clothianidin-treated sucrose solutions for 11 weeks. In this study, the NOAEC was 7.3 ng c.e./g, with effects to queen survival and colony weight observed at 14 ng c.e./g. Laycock et al. 2014 exposed microcolonies (workers without a queen) of *B. terrestris* to a thiamethoxam in syrup for 17 days, while also feeding clean pollen. Bumblebee workers survived fewer days relative to controls when presented with syrup at 98 ng/g, while production of brood (eggs and larvae) and consumption of syrup and pollen in microcolonies were significantly ($p < 0.05$) reduced by thiamethoxam at 39 and 98 ng/g. Mommaerts et al. (2010) examined the effects of thiamethoxam to bumblebees (*B. terrestris*) from oral exposure in

sugar water for 11 weeks. Colonies exposed to 100000, 10000, 1000 and 500 ng/g thiamethoxam showed a total loss of reproduction, while at 100 ng/g the numbers of drones were significantly lower than the controls.

When considering the feeding studies for bumble bees microcolonies and full colonies exposed to clothianidin and/or thiamethoxam, no effect levels were ≤ 7.3 ng c.e./g, with lowest effect levels observed at exposures ranging 5-100 (or greater) ng c.e./g in pollen or sucrose. This effects range is encompassed by the LOAECs observed in the sucrose CFSs (*i.e.*, 34-82 ng c.e./g), suggesting that honey bees and bumble bee colonies may be impacted at similar levels. The available bumble bee and honey bee studies involved different durations, which complicates comparison of endpoints. It is unclear whether the longer durations of the available bumble bee studies (*i.e.*, ranging 9-11 weeks) compared to the honey bee CFSs (*i.e.*, 6 weeks) lead to lower NOAEC values in the bumble bee studies or if bumble bee colonies are more sensitive.

Mason bee feeding studies

In another study by Sandrock et al. (2014a), mason bees (*Osmia bicornis*) were fed artificial nectar containing both clothianidin and thiamethoxam (2.92 ng c.e./g) for approximately 40 days. Bees were allowed to forage and reproduce freely. The number of nests completed, total brood cells and offspring development were significantly decreased in the treated group compared to the control.

Honey bee tunnel studies

In a tunnel study involving foliar applications of thiamethoxam to honey dew melons (MRID 49158904), applications were made either 5 or 10 days before bloom. Colonies were confined to tunnels and exposed for 8 days. In hives exposed 5 and 10 days after the application, increased mortality to adults was observed.

Several additional tunnel studies have been submitted for clothianidin or thiamethoxam. These studies generally involved exposure to smaller (nucleus) honey bee colonies foraging on seed- treated canola, maize or sunflower within a netted enclosure (*i.e.*, tunnel) over different study durations (2-52 days). These studies generally monitored mortality and foraging activity. However, most of these studies, while serving as a line of evidence in terms of the residue information provided, have deficiencies (such as extended confinement durations, adverse weather which likely reduced foraging activity, and/or only examining a single colony) that limit their utility for evaluating potential effects. These studies are presented in **Appendices 5 and 6** (effects data classified as invalid and not used in the risk assessment).

Bumble bee tunnel/greenhouse studies

One Tier II bumble bee study is available for clothianidin and four are available for thiamethoxam. These include 6 studies with foliar sprays (to turf or tomatoes) and 2 studies with soil applications (made via drip irrigation to tomatoes).

The clothianidin study involved exposures of bumble bee (*B. impatiens*) colonies to turf with clover (Larson *et al.*, 2013). When the bees were exposed for 6 d to treated turf and clover (foliar application of 0.4 lb c.e./A), worker mortality was observed, as well as decreases in colony weight, number of adults and honey pots. In treatments that were mowed, no effects were observed.

Four studies are available for exposures of bumble bees (*B. terrestris*) following foliar applications to tomatoes. In the first study (Reber 1999a), bees were exposed immediately after an application of 0.089 lb a.i./A. In exposed hives, mortality was observed as well as reduced pollination activity. In another study (Reber 1999b), tomatoes were treated with 0.13 lb a.i./A and bees were immediately exposed after. Increased mortality was observed. In the third study (Balluf 2001), an application of 0.089 lb a.i./A was made and bees were exposed either 2, 9, 14 or 21 days after application. In the third study, no effects to mortality or other endpoints measured were significantly lower than controls. Secher *et al.* 2002 exposed bumble bees to 0.089 lb a.i./A and observed increased mortality.

Two additional studies are available that examine effects on bumble bees (*B. terrestris*) following soil applications (via drip irrigation) to tomatoes. In one study (Alarcon *et al.* 2005), bees were immediately exposed after two different application scenarios (one at 0.18 lb a.i./A or two applications at 0.089 lb a.i./A). The number of adults, larvae and pupae were lower in the treatment receiving one application of 0.18 lb a.i./A compared to the control, while no effects were observed in the treatment receiving two applications. Sechser and Freuler 2003 (MRID 49579001) examined effects to bumble bees following applications of 0.13-0.14 lb a.i./A to tomatoes. After 13 to 35 days of exposure, there were no differences between the hives exposed to thiamethoxam and the negative controls.

4.3 Tier III

Tier III represents the highest level of refinement for pollinator studies. Tier III involves full field studies, with free flying colonies placed in/near treated crop areas after treatment. These studies are intended to characterize the potential effects of a pesticide on bee colonies under actual use conditions.

The majority of the available valid full field studies for clothianidin and thiamethoxam evaluated potential effects to honey bees from seed treatments (of various crops). In addition, there are a few valid studies for thiamethoxam applications to orchards or melons. There are several major limitations in the Tier III studies, which affect their utility including: uncertainty in exposure and the origin of the pollen and nectar brought back to the hives; high variability in the data collected (including in control hives); and, lack or replication or pseudo-replication. The absence of information on potential impact to overwintering is another limitation. All of these studies were classified as supplemental or qualitative due to their limitations. When considering the role of the available Tier III studies in this risk assessment, the valid studies are considered as lines of evidence for a given use pattern (*e.g.*, seed treatment of corn, foliar applications to orchard crops) and chemical. When considering effects to the colony level, Tier III studies are used in conjunction with available Tier II residue and toxicity study results. These studies are discussed below.

As studies move from Tier I to Tier III, the factors influencing declines in bee health (pesticides; pests [varroa/hive beetles]; disease [viral, fungal, bacteria]; nutrition [suitably diverse sources of pollen/nectar]; bee management practices; weather; queen condition) become more relevant. In some of the studies, certain factors (*e.g.*, weather, nutritional deficits) were likely dominant and were reflected in controls.

Honey bee colony studies for seed treatments

For clothianidin, there were several full-field registrant-submitted studies in which honey bee colonies were placed in or adjacent to fields that contained either treated corn or canola seeds (MRIDs 46907801, 46907802, 49248301, 48298802, 48298803, and 48298804), no significant differences ($p > 0.05$) between the treated and control sites were reported for colony development and health. In another study (Pohorecka, 2013), colonies located in seed treated corn fields had a transient increase in the amount of

brood compared to controls (which is not necessarily an adverse effect). In a study with seed treated oilseed rape (Rundolf *et al.*, 2014), there were no significant differences in the number of adult bees between the treated and control fields.

For thiamethoxam, there were five of studies that examined exposure after treatment of sunflower seed (at levels equivalent to application rates of 0.007-0.025 lb a.i./A), they generally reported transient effects on mortality, mostly after application, with no treatment-related effects on brood number or adult bee foraging activity (MRIDs 46163102, 46163103, 46241601, 46163103a, and 46163103b). In a study conducted using treated oilseed rape seeds (at levels equivalent to application rates of 0.033 lb a.i./A), increased honey bee mortality was observed. In Thompson *et al.* 2016, no clear treatment-related trend was observed for the measured endpoints (*i.e.*, lifespan, foraging homing activity) from treated oilseed rape seeds containing 0.02 mg a.i./seed. In Tremolada *et al.* 2010, which examined sowing operations with treated corn seeds (at application rates equivalent to 0.0065 lb a.i./A), mortality observed in the control hives and the treatment hives were similar on the day of sowing, but transient increases in bee mortality occurred immediately after sowing in the thiamethoxam treatment group. However, except for the day of sowing, the control hives had higher mortality on all other days compared to the treatment hives.

Honey bee colony studies for orchard crops

In a foliar study with pears and a soil treatment with melons treated with thiamethoxam, increased mortality of adults was observed for applications made within days of bloom.

Bumble bee colony studies for seed treatments

Cutler *et al.* 2014, examined bumble bee (*B. impatiens*) colony responses when placed adjacent to clothianidin and/or thiamethoxam seed-treated (conventional fields) or reported organic corn fields. The number of workers was significantly ($p < 0.05$) reduced ($\downarrow 25\%$) in the neonicotinoid-treated fields (combined trials) compared to the organic fields, and while not significant ($p > 0.05$), worker and drone weights were reduced by more than 25%. In the study by Rundolf *et al.*, 2014, oilseed rape seeds were treated with clothianidin. For *B. terrestris* L colonies placed adjacent to the treated fields, there was a significant decrease in the mean number of queen and worker/male cocoons per colony and a decreasing change and rate of growth (weight).

There were also studies where bumble bees were exposed following seed treatments of thiamethoxam. Wilkins 2014 (49589501) examined effects on bumble bees exposed to flowering rape grown from seeds which were treated with thiamethoxam and seeded at a rate equivalent to 0.02 lb a.i./A. No significant effects were observed in the treatment group compared to the control. Thompson *et al.* 2015 examined development of bumblebee (*B. terrestris audax*) colonies where bees had foraged for 5 weeks on flowering winter oilseed rape grown from seed treated with thiamethoxam. This study reported an increase in colony mass and foraging activity as well as a higher number of queens/gynes, workers, eggs, larvae but with a lower number of drones in thiamethoxam-treated fields.

Mason bee and wild bee studies for seed treatments

In a study by Rundolf *et al.*, 2014, oilseed rape seeds were treated with a clothianidin formulation (Elado® - 400 g/L) and during flowering the number of wild bees at field sites and field borders was examined. The number of wild solitary bees per flower was reduced in the treated field and field borders. *O. bicornis*

colonies placed in the adjacent to oilseed rape fields had reduced median number of brood tubes (6/8 females in control and 0/8 females in treated group started to build brood cells).

4.4 Incident Reports

The Office of Pesticide Programs (OPP) maintains a database called the Incident Database System (IDS) in which wildlife incidents reported to the Agency from a variety of sources are maintained. For some of these incidents in IDS, a narrative of an incident is available which reports information such as magnitude of the number of organisms impacted, location, date, product used, use pattern, whether the use was a registered use, and any confirmatory residue analysis if available. The sources of information for incidents include: registrant reports submitted under the Federal Insecticides, Fungicides, and Rodenticides Act (FIFRA) §6(a)(2) reporting requirement; reports from local, state, national and international-level government reports on bee kill incidents; news articles; and, correspondence made to EFED by phone or via email (through [[HYPERLINK "mailto:beekill@epa.gov" \h](mailto:beekill@epa.gov)]) generally reported by beekeepers and the general public.

It is noted that not all reported incidents are associated with narrative or analytical information that definitively links thiamethoxam or clothianidin exposure to the bee kill event. Analytical information can include residue analysis of dead bees observed at a site or residues in pollen and nectar that confirm thiamethoxam or clothianidin was present. Even in those cases, many incident reports are associated with findings of other pesticides, of which the interactions with thiamethoxam or clothianidin in contributing to bee kills may not be fully understood. In other instances, thiamethoxam or clothianidin were only suspected to be the cause of bee kill events based on observational accounts between beekeepers in a given area. These accounts are not always supported by a confirmatory residue analysis or apiary inspector examination of colony health. Typically, the reported wildlife incidents in general serve as a line of evidence in determining the potential effects of pesticides, as the reports are useful in understanding how these chemicals may impact non-target organisms under the actual use conditions. Much of the incident information made through phone and email correspondence to EFED does not usually include a thorough investigation of the incident or provide any confirmatory residue data to link a specific chemical with a particular incident; therefore, many of these reports are anecdotal in nature. The aggregate incident database was not searched because that database lumps all non-target wildlife (e.g. mammals, fish, invertebrates) into one category and does not distinguish between them. Since this is a refined risk assessment centered on bees, it was not deemed informative to the lines of evidence.

4.4.1 Clothianidin

A review on May 2, 2019 of the IDS database indicated a total of 54 reported ecological incidents affecting bees in the United States associated with the use of clothianidin. The incidents associated with clothianidin use that are recorded in IDS occurred between 2010 and 2018. Most of the incidents involved managed honey bees (these incidents are summarized in **Table 4-4**). The certainty categories²³

²³ The Ecological Incident Information System (EIIIS) used by EPA to store incident data relies on the following certainty indices:

- **Definite:** (residues detected in affected organisms and other lines of evidence support cause)

regarding the likelihood that the use of clothianidin caused the incidents ranged from unlikely to highly probable. The attribution of the reported effect to the clothianidin use was considered highly probable in 15 incidents (44%), probable in 16 incidents (30%), possible in 14 incidents (26%) and unlikely or not determined in 8 cases (15%). Considering all reported incidents, 19 (35%) of the incidents were considered to be associated with registered uses of clothianidin at the time of the incident, but the legality of use (*e.g.*, undetermined) was not determined in 34 (63%) of the reported incidents and a single incident was considered a misuse (not reported in **Table 4-4**). Some of the incidents involved additional chemicals besides clothianidin; in some cases, the concentrations are orders of magnitude higher for some of the other chemicals. In the incidents where clothianidin was considered probable or highly probable to have resulted in the incident, clothianidin residues were reported in several cases with residues ranging from the LOD (limit of detection) to 400 ppb in dead bee samples and several thousand ppb in foliage samples. The reported incidents for clothianidin involved uses that are currently registered (*i.e.*, corn, cotton, canola, and sugar beet), and the remaining incidents had more general use sites such as agricultural area, residential, and urban or did not have a use site specified.

In cases where entire honey bee colonies were affected, it is uncertain whether the colony-level effect was due directly to pesticide exposure, whether it was indirectly due to pesticide exposure (*e.g.*, large losses of forage bees from pesticide exposure leading to the colony being more susceptible to disease and/or starvation), or whether the effect was not related to pesticides at all but was the result of disease and/or starvation. While 27 (50%) of honey bee kill incidents reported in **Table 4-4** were associated with corn (and were generally associated with dust-off exposure following seed treatments), there is uncertainty whether insecticides, and in particular clothianidin, were in use since residues were either not measured or were not detected in several of these bee kills. Additionally, there were several other incidents (not included in **Table 4-4**) that occurred in 2012 around the time of corn planting, but formal investigations of these incidents have not yet revealed any residues of clothianidin or other neonicotinoid insecticides. Of the 27 reported corn incidents with bee kills associated with clothianidin, all but four occurred prior to 2015.

Table 4-4. Ecological Incidents Involving Bees in the U.S. Associated with Clothianidin.

Species	Legality of Use (# of incidents)	Use Site (# of incidents)	Response	Effects/Notes
<i>Apis</i> (honey bee)	Registered (18)	Corn (9)	Mortality	Bee Kills ranging from 100s of individual bees to many colonies.
		Agricultural Area (6)		Individual bees to 12 hives. Five of these incidents were associated with corn seed planting.
		Potato (2)		1 hive each. Aerial foliar applications.
		Residential (1)		Dozens of bees. Soil treatment to trees.

- **Probable:** (residues were not measured or the measured residues were not sufficient to be considered toxic, but pesticide was used in close proximity and would be capable of exerting such an effect)
- **Possible:** multiple pesticides were used in close proximity and any of them are capable of causing such an effect.
- **Unlikely:** there are no measured residues and the observed effects are not consistent with those caused by pesticides used in the area or there was no pesticide use known in the area.
- **Unrelated:** effects observed in the incident are unrelated to pesticide use.

	Undetermined (33)	Agricultural Area (5)		Single hive to 800 colonies affected. Four of these incidents were associated with corn seed planting.
		Corn (9)		100s of individual bees to up to 1300 hives affected
		Cotton (3)		Up to 50% of worker bees
		Residential (1)		1 hive
		Unknown/Not reported (15)		Up to 48 colonies.
Bumble bee (<i>Bombus</i> sp)	Registered (1)	Urban (1)	Mortality	Extent Not reported. Application was to ornamental trees.
	Undetermined (1)	Not Reported (1)		>1000 dead bees. Application was made to ornamental trees.

4.4.2 Thiamethoxam

From 2002-2018, twenty-two incidents have been reported in the US for honey bees in association with agricultural uses of thiamethoxam. Seven (33%) of the incidents with certainties of highly probable or possible have been reported in association with corn planting in IN, MN and IL. Observations included hundreds to thousands of dead bees and bees with behavioral impacts. Twelve incidents considered probable or possible were reported by the state of Washington in 2002 in association with applications of thiamethoxam to orchards (as unspecified, or to pears or cherries). In most of these incidents, the bee hives were located within the treated orchards. In addition, an incident was reported in CA in association with thiamethoxam applications to lemon trees. In 2018, an incident was reported in association with an application to watermelons. One additional incident was associated with applications to an “agricultural area”. Incident reports associated with agricultural uses of thiamethoxam with certainties rated “highly probable”, “probable” or “possible” that occurred in the US are included in **Table 4-5**; all of these incidents involved honey bees.

Table 4-5. Reported bee incidents in the US involving agricultural uses of thiamethoxam.

Incident #	Crop	Legality *	Certainty*	State	year	Residues* **	Effects
I022340-001	Agricultural area	U	Ps	IN	2010	C	thousands of dead and drunk-looking bees on grass and in front of hives at four apiaries
I020998-001	Cherry orchard	R	Ps	WA	2002	NR	moderate bee kill
I020998-003	Cherry orchard	U	Ps	WA	2002	NR	Bee kill
I023902-001	Corn (seed)	U	HPr	IN	2012	T and C	33 nucleus colonies were exhibiting dead/dying bees at the entrances of the colonies
I025176-001	Corn (seed)	U	HPr	MN	2013	T	Dead bees in front of hives. Some bees were crawling on the ground unable to fly and others exhibited trembling and twitching

							on their backs unable to right themselves.
I025271-001	Corn (seed)	M	HPr	MN	2013	T and C	dead bees quivering or dead in front of 900- 1,000 hives
I026468-001	Corn (seed)	U	HPr	IN	2014	T and C	dead bees
I025208-001	Corn (seed)	U	Pr	IL	2013	NR	dead bees around 20-25 hives
I028123-002	Corn (seed)	U	Ps	IN	2015	T and C	1500 dead bees
I023967-001	Corn, field	U	Ps	MN	2012	T and C	Bee kill involving 1,346 hives
I027610-001	Lemon	R	Ps	CA	2015	NR	dead bees observed in 134 of 400 hives
I020998-002	Orchard	M	Pr	WA	2002	NR	slight to moderate bee kill
I020998-004	Orchard (unspecified)	U	Pr	WA	2002	NR	Bee kill
I020998-005	Orchard (unspecified)	U	Pr	WA	2002	NR	Bee kill
I020998-017	Orchard (unspecified)	R	Ps	WA	2002	NR	Bee kill
I020998-018	Orchard (unspecified)	R	Ps	WA	2002	NR	Bee kill
I020998-019	Orchard (unspecified)	R	Ps	WA	2002	NR	Bee kill
I020998-020	Orchard (unspecified)	R	Ps	WA	2002	NR	Bee kill
I020998-021	Orchard (unspecified)	R	Ps	WA	2002	NR	Bee kill
I020998-006	pear orchard	U	Pr	WA	2002	NR	Bee kill
I020998-016	pear orchard	R	Ps	WA	2002	NR	Bee kill
I031569	Watermelon	U	U	CA	2018	T	Bee kill

*U=undetermined, R = registered use, M = misuse

**HPr= highly probable, Pr= probable, Ps=possible

***T= thiamethoxam, C= clothianidin, NR = not reported

5 Risk Characterization

5.1 Tier I Analysis

For crop uses where an exposure potential of bees is identified, the next step in the risk assessment process is to conduct a Tier I risk assessment. By design, the Tier I assessment relies on conservative (high-end) estimates of exposure via contact and oral routes. For contact exposure, only the adult (forager) life stage is considered since this is the relevant life stage of honey bees for contact exposure. Effects are defined by

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laboratory exposures to groups of individual bees. Estimated exposure values are compared to toxicity endpoints to derive risk quotients.

As previously described (**Section 2**) a total residues approach is being adopted for thiamethoxam to encompass potential exposure and toxicity to both thiamethoxam and its major degradate clothianidin and where clothianidin is applied directly. Consequently, as previously mentioned all application rates and subsequent exposure values are expressed as clothianidin equivalents (c.e.) for risk estimation from both chemicals. For soil applications fate properties for clothianidin ($\log K_{ow}$ 0.64 and K_{oc} 160) are used for all scenarios given exposure values are in terms of c.e. Additionally, because of the similar toxicity of both chemicals to individual bees, tier 1 RQs are calculated based on the most sensitive endpoint available (for either chemical). No notable difference occurs in the risk conclusions (based on LOC exceedances) when using clothianidin or thiamethoxam's fate properties or toxicity information.

The endpoints used for the RQs presented in this section represent the most sensitive adult acute contact (thia) LD50 of 0.021 $\mu\text{g c.e./bee}$, adult acute oral (clothi) LD50 value of 0.0037 $\mu\text{g c.e./bee}$, and adult chronic (clothi) NOAEL of 0.00036 $\mu\text{g c.e./bee/day}$. For larvae, there are no acceptable definitive acute oral toxicity studies for clothianidin or thiamethoxam. However, there is an acceptable larval chronic toxicity study with thiamethoxam from which the day 4 dose and corresponding 8-day mortality endpoint will be used for the acute oral toxicity estimate. This value is non-definitive at $>0.025 \mu\text{g c.e./bee}$. For chronic toxicity to larvae a NOAEC for thiamethoxam at 0.024 $\mu\text{g c.e./larvae/day}$ is available. There are no data considered adequate to calculate dose-based Tier I RQs for clothianidin, and the thiamethoxam endpoint was used to estimate chronic RQs for larvae.

As with the Tier 1 exposure section (**Section 3.5**) the discussion below is based on bracketing maximum and minimum labeled application rates for each of the chemicals and includes non-agricultural uses. A refined Tier I and additional Tier II analyses have been performed for each chemical separately

5.1.1 On-field Contact Exposure to Adult Bees (Foliar Uses Only)

Table 5-1 summarizes the screening-level acute contact RQ values for adult honey bees that are assumed to be foraging on a bee-attractive crop during pesticide application. RQs are relevant only to those crops that are considered bee attractive or for which no data are available on bee attractiveness (**Tables 3-6-3-8**). For all foliar uses assessed, acute contact RQ values range from 5.1 to 52 (0.04 lbs c.e./A to 0.41 lbs c.e./A respectively) and exceed the Agency's acute risk LOC of 0.4.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Summary of Tier I screening-level RQs for contact exposure ranges resulting from foliar uses of clothianidin and thiamethoxam (screening-level contact on-field)

Chemicals	Max. Single Appl. Rate (lbs c.e./A) ^a	Dose ($\mu\text{g c.e./bee}$) per 1 lbs. a.i./A)	Clothianidin Contact Dose ($\mu\text{g c.e./bee}$)	Acute Contact RQ ^b
Thiamethoxam	0.04	2.7	0.11	5.1
Clothianidin and Thiamethoxam ^c	0.08	2.7	0.22	11
	0.2	2.7	0.54	26
Clothianidin	0.4	2.7	1.1	52

^a Thiamethoxam application rates are converted to clothianidin equivalents (c.e.)

^b Based on a 96-h acute contact LD50 of 0.021 $\mu\text{g c.e./bee}$ for thiamethoxam (MRID 44714927)

c the upper bound of a thiamethoxam app rate is 0.23. RQs are presented for the clothianidin app rate for brevity. Risk conclusions are unchanged by the difference in this rate at the Tier I level.

Bolded value exceeds the acute risk LOC of 0.4

5.1.2 Screening-level Dietary RQs for On-field (Foliar, Soil and Seed treatments)

Oral Exposure (Foliar and Soil Treatment Uses)

For oral (dietary) exposure, the Tier I assessment initially considers just the caste of bees with the greatest oral exposure (nectar foraging adults). If risks are identified, then other factors are considered for refining the default Tier I risk estimates. These factors include other castes of bees and available information on residues in pollen and nectar which are deemed applicable to the crops of interest. Oral exposure through the consumption of clothianidin-contaminated pollen is considered for on-field and off-field scenarios resulting from foliar applications. For soil and seed- treatment applications, where no spray drift is expected (this excludes potential dust-off from seed treatment), oral exposure is assessed for the on-field scenario only.

Table 5-2 below summarizes the on-field acute and chronic oral RQs resulting from a range of the foliar and soil application rates of clothianidin and thiamethoxam. The acute and chronic RQs for adult bees exceed the LOCs of 0.4 and 1, respectively, for all use patterns assessed. Adult acute RQs ranged from 350 – 3,600 for foliar applications and 1.2 – 7.0 for soil applications, while adult chronic RQs ranged from 3,600– 36,000 for foliar applications and 13 – 70 for soil applications. Larval chronic RQs also exceeded the chronic LOC (1) for all foliar applications ranging from 300-1500, while they were below the chronic LOC for clothianidin soil applications (but not thiamethoxam soil aps). There is one notable apparent difference in toxicity endpoints between thiamethoxam and clothianidin, as the adult chronic endpoint is an order of magnitude different between clothianidin and thiamethoxam. For foliar and soil applications, if the thiamethoxam adult NOAEC (0.024 µg c.e./bee) were used to calculate RQs they would decrease by about an order of magnitude. Additionally, for soil applications, if the thiamethoxam fate properties (log k_{ow} -0.13 and k_{oc} 70.2) were considered RQs would generally increase by less than a factor of 2X. Because there would be no new exceedances using the most sensitive toxicity endpoints for adults and the clothianidin fate properties were considered to give a reasonable estimate.

Table [STYLeref 1 \s]-[SEQ Table * ARABIC \s 1]. Summary of Tier I RQs for Dose-Based Oral Exposure to Adult and Larval Honey Bees Resulting from Foliar and Soil Uses of Clothianidin and Thiamethoxam Based On Model- Generated Exposure Values On-Field)

Chemicals	Max. Single Appl. Rate (lbs c.e./A) ^a	Dose (µg c.e./bee per 1 lbs. a.i./A)	Clothianidin Oral Dose (µg c.e./bee)		Acute RQ ^b	Chronic	
			Adult	Larvae		Adult ^c	Larvae ^d
Foliar Applications							
Thiamethoxam	0.04	32	1.3	0.54	350	3,600	300
Clothianidin/ Thiamethoxam ^e	0.08	32	2.6	1.1	690	7,100	600
	0.2	32	6.4	2.7	1,700	18,000	1,500
Clothianidin	0.44	32	5.6	13	3,600	36,000	1,300
Soil Applications							
Clothianidin and Thiamethoxam ^e	0.09	0.05	0.005	0.002	1.2	13	0.5
	0.2	0.05	0.01	0.004	2.8	28	0.9
Clothianidin	0.4	0.05	0.02	0.009	5.6	57	2.1

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Clothianidin	0.49	0.05	0.03	0.01	7.0	70	2.3
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^a Thiamethoxam application rates are converted to clothianidin equivalents (c.e.)

^b Based on a 48-h acute oral LD50 of 0.0037 µg c.e./bee for clothianidin (MRID 45422426).

^c Based on adult 10-day chronic NOAEC of 0.00036 µg c.e./bee for clothianidin (MRID 48414901).

^d Based on larval 21-day chronic NOAEC (emergence) of 0.0043 µg c.e./bee for thiamethoxam (MRID 50096607).

^e The upper bound of a thiamethoxam app rate is 0.23. RQs are presented for the clothianidin app rate for brevity.

Risk conclusions are unchanged by the difference in this rate at the Tier I level

Bolded value exceeds the acute risk LOC of 0.4 or chronic risk LOC of 1

As noted previously, there were no quantitative acute larval toxicity endpoints with definitive LD50 values. Therefore, acute dose-based RQs were not calculated for larvae. However, comparing the non-definitive 8-day larval LD50 from the chronic thiamethoxam study (>0.03 µg c.e./larvae; 5% mortality) the larvae dose 0.54 (µg c.e./larvae) at the lowest foliar application rate would require the almost two orders of magnitude less sensitive to be below the acute larval LOC. Thus, risk is considered likely to acute larvae exposure from foliar applications. For soil application rates, where would be no exceedances based on assuming the lowest values of 0.03 µg c.e./larvae, at any application rate. This risk pattern is like that observed for chronic exceedances.

For clothianidin, the quantitative chronic oral toxicity study for honey bee larvae exposed to clothianidin (MRID 48876801) was unable to determine a dose-based endpoint. For comparison to the exceedances generated by the thiamethoxam endpoint, chronic risk to honey bee larvae was further characterized (for clothianidin) by directly comparing modeled and measured residues in pollen and nectar to the larval 22-day chronic NOAEC of 0.680 µg c.e./g- diet. Using this approach, the chronic risk LOC of 1.0 for larval bees was exceeded for all foliar use patterns but (**Table 5-2**) did not exceed the chronic risk LOC for soil applications. For foliar applications estimated concentrations of clothianidin ranged from 8,800 – 45,000 (ng c.e./g) which are 1-2 orders of magnitude greater than the endpoint of 608 ng c.e./g- diet (MRID 48876801), suggesting chronic risk concerns for larvae. For soil applications, estimated concentrations of clothianidin ranged from 16 – 86 (ng c.e./g) which are an order of magnitude less than the endpoint of 608 ng c.e./g- diet, suggesting no chronic risk concerns for larvae from soil application. These conclusions mirror those when using the thiamethoxam endpoints.

Screening Level RQs for Applications of Poultry Litter from Treated Broiler Houses to Agricultural Fields

As described above in the Tier I Screening-level RQs section, the maximum application rate assessed for soil applications of clothianidin was 0.49 lb a.i./A, based on applications of poultry litter manure to agricultural fields that had previously received clothianidin applications in poultry houses and resulting RQs calculated in Bee-REX were as high as 7.0 and 70 for acute and chronic risks, respectively to adult bees. Chronic risk was not expected for larval bees (RQ of 0.4). Calculation of the maximum rate is described here as well as the effect of proposed label language intended to mitigate potential risks.

For poultry house use, the chicken litter waste collected from the broiler house could potentially be disposed of as a soil amendment after it has been treated with clothianidin. To assess the impacts of clothianidin -treated poultry litter used as soil amendments, EFED modeled the amount of clothianidin predicted to be in the poultry litter, as if it were applied to a corn field prior to planting. The poultry house use pattern evaluated by EFED represents an upper-end use pattern for products applied to poultry houses. The primary pest targeted by these products is the darkling beetle, which is mostly found on the perimeter portions of floors and lower walls, near feeders and water lines. While only portions of a poultry

house may need to be treated, this is not explicitly stated or restricted on the current product label. For modeling the highest exposure scenario, EFED conservatively assumed that the whole poultry house was treated each time a treatment is made. Treatments are made prior to a new flock occupying the poultry house, and it is assumed that annually, six broiler flocks will occupy a house. Although treatments are made, removal of the litter from the house may not occur, and fresh litter will be placed on top of existing litter. For broilers, this means that six whole house treatments could occur prior to an annual litter clean out, with multiple layers of treated litter possible. An application rate for clothianidin-treated manure on a corn field was developed using the following process based on previous EPA risk assessments regarding this exposure pathway (USEPA, 2012):

- a. Application rate for Darlex (EPA Reg. No. 1021-2771) - 4 oz of Darlex/1000 ft²; treating a 20,000 ft² house (maximum size poultry house) = 80 oz Darlex.
- b. Darlex contains 23.6% w/w clothianidin a.i. 80 oz Darlex = 1.33125 lb clothianidin.
- c. A typical broiler house has six whole house treatments (6 flocks of broilers) before a full litter clean out, followed by storage, then application on a corn field. Treatment of 6 flocks results in application of 7.9875 lb of clothianidin (6 x 1.33125 lb a.i./application).
- d. Six flocks will produce 168 tons of manure, and require 35 tons of bedding, resulting in a total of 203 tons of litter.
- e. The cumulative residual concentration of clothianidin in litter is 7.9875 lb/203 tons litter = 0.039347 lb a.i./ton litter.
- f. Maximum elemental nitrogen requirement for corn is 220 lb plant available nitrogen per acre (N/A)
- g. Six flocks of broilers produce 14,400 lb nitrogen; 45% of this is assumed/estimated to be lost during storage, resulting in 7920 lb of nitrogen.
- h. Only 90% of the nitrogen is available to plants in the first year (USDA estimate of mineralization), resulting in 7128 lb of plant available nitrogen.
- i. An additional 50% of the nitrogen is lost during application, resulting in 3564 lb plant-available nitrogen.
- j. Based on the nitrogen application rate of 220 lb N/A, this results in 16.2 A being needed for the manure from six flocks (3564 lb N/220 lb N/A = 16.2).
- k. Based on a cumulative litter production of 203 tons, this results in a litter application rate of 12.5 tons/A (203 tons litter/16.2 A = 12.5 tons litter/A).
- l. Based on a residual clothianidin concentration in litter of 0.039347 lb a.i./ton litter, and a litter application rate of 12.5 tons/A, the outdoor equivalent application rate for clothianidin is 0.49 lb a.i./A.

Twelve alternative poultry house clothianidin treatment scenarios were suggested by the registrant (MRID 49681202) and BEAD (USEPA 2017b) for modeling and were also considered in the preliminary non-pollinator ecological risk assessment (USEPA, 2017c). Given clothianidin's persistence, no degradation was assumed to occur between collection of the litter and its application to a field. In examining potential risk to bees from clothianidin-treated litter applied as soil amendments, the Agency is considering the maximum application rate/conservative assumptions scenario described above (equivalent to 0.49 lb a.i./A) as well as potentially mitigating exposure by requiring the following label mitigation for applications to poultry houses:

"Limit applications to one whole house treatment and 5 perimeter (partial house) treatments per year. Do not apply more than 5 tons of litter treated with Darlex per acre per year."

This label mitigation would decrease the outdoor equivalent application rate for clothianidin to 0.0845 lb a.i./A and is identical to Run 8 in the non-pollinator ecological risk assessment (USEPA, 2017c). Under this mitigation scenario, the acute and chronic LOC for a field receiving clothianidin -treated poultry litter used as soil amendments would still be exceeded (Bee-REX Tier I screen calculated acute and chronic adult bee RQs of **1.2** and **12.0**, respectively, based on the 48-hr acute oral LD₅₀ of 0.0037 µg c.e./bee and the 10-D chronic NOAEC of 0.00036 µg c.e./bee).

Additional Considerations

Poultry litter is commonly used as a fertilizer supplement on pastures, forages, and agronomic crops such as cotton and corn. In the case of corn, which typically receives the highest rates of litter application other than pastures and some vegetable production (USEPA, 2017b), the corn crop only produces honey bee attractive pollen. Therefore, when using the proposed mitigation label language and considering bee exposures restricted to only pollen containing clothianidin residues following applications of treated poultry litter as a soil amendment to corn fields, the resulting acute and chronic RQs would be below the LOCs (Bee-REX screening level acute and chronic dietary RQs of 0.01 and 0.10, respectively).

It is notable that exposures and resultant RQs may be higher than indicated here where poultry litter containing clothianidin residues is applied on top of fields receiving other registered clothianidin applications (*e.g.*, seed-treated corn or foliar-treated cotton).

Overall, the available information suggests potential for risks of concerns for bees from fields receiving treated poultry litter at either the currently registered or proposed mitigation rates based on exceedances of the clothianidin Tier I adult bee endpoints. Given the various uncertainties regarding applications of treated poultry litter, including the low overall adoption of clothianidin usage in poultry houses (USEPA, 2017b) and the large range of potential application sites, a Tier II analysis of this use pattern was not conducted.

Oral Exposure (Seed Treatment Uses)

All RQs (adult acute oral [79], adult chronic oral [810], and larval chronic oral [29]) exceed the acute and chronic risk LOCs of 0.4 and 1, respectively (**Table 5-3**).

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Summary of acute and chronic risk quotients (RQ) for adult bees from seed treatment applications of clothianidin and thiamethoxam (screening-level oral on-field)

Use pattern	EEC in pollen and nectar	Oral Dose (µg c.e./bee) ^a		Adult Acute RQ ^b	Chronic RQ	
		Adult	Larvae		Adult Chronic RQ ^c	Larval Chronic RQ ^d
All registered seed treatment use patterns	1 µg c.e./kg (screening-level value for all seed treatment uses, 0.2 lb c.e./A)	0.292	0.124	79	810	29

^a Source: USEPA et al. 2014. Guidance for Assessing Pesticide Risks to Bees. Used for the dose-based adult endpoints

^b Based on an adult 48-h acute oral LD₅₀ of 0.0037 µg c.e./bee for clothianidin (MRID 45422426).

^c Based on adult 10-day adult chronic NOAEC of 0.00036 µg c.e./bee (MRID 48414901).

^d Based on adult 21-day larval chronic NOAEC of 0.0043 µg c.e./bee (MRID 50096607).

For the non-definitive acute larval endpoint, the nondefinitive toxicity value ($>0.03 \mu\text{g c.e./larvae}$) would have to be over an order of magnitude greater to not exceed the acute LOC. Additionally, considering dietary concentration for clothianidin, the dietary EEC of $1 \mu\text{g c.e./kg}$ in nectar and pollen was used and is greater than the NOAEC value of $0.680 \mu\text{g c.e./g-diet}$ (1.5X greater).

5.1.3 Off-Field Screening Level RQs (spray drift transport from foliar applications)

As described in **Section 3**, clothianidin and thiamethoxam products may be applied to crops via foliar spray applications. Consistent with the Agency's risk assessment process for bees and other taxa, exposure beyond the treated field is expected to occur as a result of spray drift. This "off-field" exposure is assessed here for honey bees that are assumed to be foraging adjacent to treated fields. The AgDRIFT model (v. 2.1.1²⁴) is used here to estimate the fraction of the foliar-applied application rate at various distances beyond the treated field. The AgDRIFT model accounts for multiple factors that affect the distance and amount of spray drift (and consequently the associated risk) of a single spray application. These include factors such as wind speed, spray nozzle type, and release height.

AgDRIFT scenarios were modeled that span the range of foliar spray application rates presented in **Section 5.1.1** (Tier I Contact) in order to bracket the potential for off-field risks. Default inputs such as droplet size were used in this modeling exercise. In addition, the default Tier I acute and chronic RQs for the honey bee were used to determine the distance required to no longer exceed the acute LOC (0.4) or chronic LOC (1.0). In modeling using AgDRIFT, default conditions were used, except for the variations mentioned in the following paragraphs and/or in the tables and footnotes.

Ground applications were modeled using AgDRIFT in Tier I ground mode with a range of ground application rates and the default droplet size (very fine to fine) with a high boom height. Results indicate that contact RQ values exceed the acute risk LOC from 33- 300 ft. beyond the treated field. Aerial applications were modeled using AgDRIFT in Tier I Aerial mode with default droplet size (fine to medium). Results indicate that contact RQ values exceed the acute risk LOC from 120 to 630 ft. beyond the treated field. Acute and chronic Tier I dietary-based RQ values exceed their respective LOCs for more than 1000 ft. from the edge of the treated field for both ground and aerial applications. Chronic exceedances are based on repeated exposures at the same concentration and do not take into account the degradation of the chemical. Consequently, without considering how long residues remain to trigger the chronic risk LOC, there is some uncertainty regarding the chronic of off-field risks. Additionally, the AgDrift model assumes that there is no interception by a crop canopy and that winds are unidirectional and constant. Results are presented below in **Table 5-4**.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Tier I Distances RQs exceed the acute risk LOC (0.4) and chronic risk LOC (1.0) for bees from ground and aerial applications of clothianidin and thiamethoxam at various rates, 90th percentile results.

Chemical	Ground Applications ^a			
	Application Rate ^c	Acute Contact (fraction applied) ^d	Acute Oral	Acute Chronic
Thiamethoxam	0.04	33 (0.078)		

²⁴ 15 Available at [HYPERLINK "http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment" \l "atmospheric" \h] (accessed 11/8/15).

Clothianidin/Thiamethoxam	0.08	72 (0.036)	>1000	
Clothianidin	0.2	165 (0.015)		
Clothianidin	0.4	299 (0.0076)		
Aerial Applications ^b				
Chemical	Application Rate ^c	Acute Contact (fraction applied) ^d	Acute Oral	Acute Chronic
Thiamethoxam	0.04	122 (0.078)	>1000	
Clothianidin/Thiamethoxam	0.08	256 (0.036)		
Clothianidin	0.2	634 (0.015)		
Clothianidin	0.4	>1000 (0.0076)		

^a For ground applications, the default droplet size is very fine (VF) to fine (F); and high boom height were used.

^b For aerial applications, the default droplet size of fine to medium was used.

^c The model also assumes for application there is no interception by a crop canopy and that winds are unidirectional and constant.

^d Fraction applied = LOC/RQ and is the application rate estimate at the distance listed required not to exceed an LOC. It is presented only for Acute contact distances because the other are greater than 1000 ft.

5.1.4 Refined Tier I Dietary RQs

To refine default Tier I risk estimates, available measured residue data in pollen and nectar are used to evaluate oral exposure (contact exposure not considered in refined estimates) and further characterize risk for other castes of bees using their food consumption rates. These refined exposure estimates in pollen and nectar are then compared to the Tier I (*i.e.*, individual level) toxicity endpoints analogous to the process using the model-generated or default Tier I exposure estimates. While RQs presented in the default Tier I assessment are based on highest exposure estimates for contact and/or dietary exposure routes (*i.e.*, exposure to workers foraging for nectar and exposure to 5-day old larvae), the Bee-REX model also calculates dietary exposure values and associated RQs for larvae of different ages, adult workers with different tasks (and associated energy requirements) and the queen using those different food consumption rates. Consequently, a potential spectrum of risk estimates is available for multiple castes and life-stages of honeybees.

Presented below in the **Sections 5.1.4.1.** and **5.1.4.2** is a summary of RQs resulting from using available measured residues in pollen and/or nectar for use patterns of clothianidin and thiamethoxam from foliar and soil applications. For the purposes of this assessment, the refined Tier I RQs presented below are the maximum. The range of RQs and where multiple crops are available in a single crop group calculated by Bee-REX are presented in **Appendix 7**. This was done because any exceedance²⁵ of the LOCs for dietary exposure at the Refined Tier 1 level was considered to warrant an evaluation of risks at the colony level where available residue data exists. For adult acute oral RQs, the acute EECs (maximum measured concentration among all individual replicates following application) and the chronic EECs (maximum average concentration among all individual sampling events following application) are compared against the same acute and chronic toxicity endpoints used in the default Tier I assessment using clothianidin and thiamethoxam toxicity endpoints. Although Bee-REX includes consumption rates for royal jelly, residue information for this matrix is not available from any residue study for either chemical. As royal jelly constitutes the exclusive diet of the larval and adult queen and for 1-3 day-old worker and drone larvae, refined Tier I oral RQs are not available for the queen (larval and adult) or 1-3 day-old worker larvae.

²⁵ This includes considering adult vs larval exceedances. For many uses there are no larval exceedances, where there are for adults and a colony level analysis was performed here. For clothianidin, there are no dose based endpoints for larval honeybees,

This Tier I refinement also considers the RQs exceedances at different times based on measured residues at distinct time points. The RQs are based on residues of both pollen and nectar where data are available, and may reflect time points over the course of a single or multiple season, depending on study designs. Due to differences in study designs (*i.e.*, if residues were measured at multiple times over the course of the season or once yearly), estimates for how long an RQ exceeds the LOC are not available for every study/crop where empirical residue values are available. This information is summarized in **Tables 5-5 and 5-6** below, and the graphical representation of all crops (where available) is located in **Appendix 7**.

Some additional considerations when evaluating Tier I (refined) risks include:

- The possibility of exposure considering the attractiveness of the crop not only to honey bees but other species of bee, and if bee pollination is required.
- If crops are harvested prior to bloom for on-field vs. off-field risks.
- Some RQs may be based on only one matrix. This may be because, only one matrix is considered honey bee attractive (*e.g.*, corn pollen), the plant doesn't produce a specified matrix (*e.g.*, potato and nectar) or the data are not available. Anthers have been used as a surrogate for pollen where those data are available and pollen data alone are not available.
- Off-field risk is expected wherever on-field risk is identified; however, distances off the fields are not updated (from **Section 5.1.3**) based on Refined Tier I RQs. Certain crop matrices, are not considered attractive to honeybees but are considered attractive to other non-*Apis* species. On-field risks not identified for honeybees, based on attractiveness does not preclude the potential for risks off field to non-*Apis* species if LOCs are exceeded.

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5.1.4.1 Clothianidin – Foliar and Soil Applications

Table 5-5 presents the refined Tier 1 RQs for clothianidin for available residue data. If crops group are not considered attractive or data are not available they are not included in this table. As noted above any exceedance at this level meant proceeding to tier II analysis so no additional characterization is provided.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Summary of Refined Acute and Chronic Adult and Larval Tier I Risk Quotients (RQs) based on Measured Maximum and Mean-maximum Residues across Crop Groupings following Foliar and Soil Applications of Clothianidin.

Group #	Crop Group	Appl. Method	Crop Residue Data Used	Max EECs		Max Adult RQs		Max Larval RQs ¹	% Adult* RQs Exceeding over time	
				Acute	Chronic	Acute	Chronic	Chronic	Acute	Chronic

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1	Root and Tuber Vegetables	Foliar	Potato	Pollen-116 Nectar-0 ²	Pollen-76.1 Nectar-0 ²	0.30	2.0	0.07	0%	6%
		Soil	Potato	Pollen-188 Nectar-0 ²	Pollen-92.5 Nectar-0 ²	0.49	2.5	0.09	6.3%	19%
9	Cucurbit Vegetables	Foliar	Pumpkin	Pollen-123 Nectar-6.5	Pollen-108 Nectar-4.86	0.5	4.1	0.26	12%	28%
		Soil	Pumpkin Squash Cucumber Melon	Pollen-39.5 Nectar-65.5	Pollen-39.5 ³ Nectar-65.5 ³	5.2	53	2.16	36%	72%
10	Citrus Fruits	Soil	Orange Lemon	Pollen-631 Nectar-114	Pollen-412 Nectar-64.6	1.2	52.4	2.5	65%	98%
11	Pome Fruits	Foliar	Apple	Pollen-57.4 Nectar-0.5	Pollen-31.2 Nectar-0.5	0.18	1.10	<0.1	0%	17%
12	Stone Fruits	Foliar	Peach	Pollen-130 Nectar-0.5	Pollen-49.7 Nectar-0.5	0.36	1.4	<0.1	0%	17%
13	Berry and Small Fruit	Foliar	Grape	Pollen-1564 Nectar ² -0	Pollen-1306 Nectar ² -0	4.1	34.8	1.3	50%	50% (19%-L)
		Soil	Grape	Pollen-206 Nectar ² -0	Pollen-160 Nectar ² -0	0.53	4.3	0.16	25%	38%
14	Tree Nuts	Foliar	Almond	Anthers-88.1 Nectar-2.04	Anthers-43.5 Nectar-1.23	0.25	1.64	<0.1	0%	5.6%
20	Oilseed	Foliar	Cotton	Pollen-0 ³ XFNectar-4383	Pollen-0 ³ XFNectar-3364	346	2729	109.1	60%	68% (5%-L)

* Where chronic larval exceedances occur, the percentage of chronic samples exceeding the chronic larval endpoint is denoted with an (L)

¹ The available clothianidin chronic endpoint is not a dose-based endpoint. Given the similarities in the available Tier I laboratory data between clothianidin and thiamethoxam, the thiamethoxam larval endpoint of 0.0037 µg c.e./bee was used to determine Tier I chronic larval risk estimates. Therefore, chronic risk to larvae is evaluated by directly comparing the combined empirical residues in pollen/nectar with the chronic larval dietary-based endpoint.

² Tested crop species does not produce nectar. Tier I estimates may therefore underestimate potential risk posed by applications to crops within the crop group that produce attractive honey bee nectar³ Cotton pollen is unattractive to honey bees. As such, although residues in pollen were quantified in the study report, risk was assessed assuming bees were obtaining their pollen resources from other untreated plant species with uncontaminated pollen. As cotton is the only oilseed crop species

registered for soil applications, this is considered a reasonable assumption.

³ Mean and max concentrations are the same, as there was only one hand-collected sample per time point.

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4.

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4.1.1.

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4.1.4.

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5.1.4.2 Thiamethoxam – Foliar and Soil Applications

Table 5-6 presents the refined Tier 1 RQs for thiamethoxam for available residue data. If crops group are not considered attractive or data are not available they are not included in this table. Acute larval RQs

were not calculated due to non-definitive toxicity data. As noted above any exceedance at this level meant proceeding to tier II analysis so no additional characterization is provided. Bold values indicate the residues data used for the refined Tier I RQ.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Summary of Refined Acute and Chronic Adult and Larval Tier I Risk Quotients (RQs) based on Measured Maximum and Mean-maximum Residues across Crop Groupings following Foliar and Soil Applications of Thiamethoxam.

Group #	Crop Group	Appl. Method	Crop Residue Data Used	Residues (pollen and nectar)		Adult RQs		Larval RQs	% RQs Exceeding over time	
				Acute	Chronic	Acute	Chronic	Chronic	Acute	Chronic
6	Legume Vegetables	Foliar	Soybean	545 (P) 443 (N)	486 (P) 42.5 (N)	3.5	34	1.8	30	35
8	Fruiting Vegetables	Foliar	Tomato	14504 (P) None (N)	8909 (P) None (N)	38	240	1.3	56	61
		Soil	Tomato, Chili Pepper	268 (P) 1384 (N)	238 (P) 534 (N)	109	430	18	78	50
9	Cucurbit Vegetables	Foliar	Cucumber, Pumpkin	1228 (P) 297 (N)	1049 (P) 168 (N)	23	1400	56	100	89
		Soil	Melon, Cucumber	755 (P) 57.6 (N)	310 (P) 28.7 (N)	4.6	23	1.2	93	50
10	Citrus Fruits	Foliar	Orange	878 (P) 12.1 (N)	703 (P) 10.0 (N)	2.7	22	1.0	19	41
		Soil		410 (P) 65.2 (N)	107 (P) 19.8 (N)	1.9	11	0.48	71	50
11	Pome Fruits	Foliar	Apple	2124 (P) 660 (N)	1756 (P) 496 (N)	52	400	18	100	94
12	Stone Fruits	Foliar	Peach, Plum, Cherry	328 (P) 5.5 (N)	160 (P) 2.48 (N)	1.1	5.2	0.24	N/A	N/A
13	Berry and Small Fruit	Foliar	Strawberry, Cranberry, Blueberry	1932 (P) 2107 (N)	1186 (P) 1057 (N)	170	860	35	100	100
		Soil	Strawberry	1669 (P) 186 (N)	1126 (P) 86.9 (N)	15	71	3.9	89	72
20	Oilseed	Foliar	Cotton ^a	316 (P) 9.83 (N) 675 (EFN)	54.8 (P) 3.1 (N) 80.8 (EFN)	53	66	2.7	N/A	N/A
24	Other	Foliar	Ornamentals	3127 (P) 1192 (N)	1238 (P) 796 (N)	94	650	27	100	88
		Soil		3127 (P) 1192 (N)	1238 (P) 796 (N)	1.8	19	1.1	55	55

N/A – Due to study design, data were not amenable to this analysis.

^a Although cotton pollen is not attractive to honeybees residues were used in this calculation to represent all oilseed crops

5.1.4.3 Clothianidin and Thiamethoxam – Seed Treatments

As discussed in the use characterization, clothianidin and thiamethoxam are both registered for use as a seed treatment on a wide variety of seed crops. The Tier I RQs using BeeREX's default exposure assessment for seed treatments resulted in RQs that exceeded LOCs. Therefore, a refined approach is considered here.

Crops that are not bee attractive

A number of crops that are registered for seed treatments of clothianidin and thiamethoxam but are not considered attractive to honey bees (according to USDA 2017). Additionally, a number of other seed treatments are for crops that are harvested prior to bloom. Given the lack of potential exposure, there is a low likelihood of adverse effects from seed treatment uses that are either not attractive to honey bees or are harvested prior to bloom. This does not apply to crops that are grown for seed.

Seed treatment uses that are not attractive to honey bees.

- Barley
- Oat
- Potato
- Spinach
- Rice
- Rye
- Triticale
- Wheat

Seed treatment uses that are harvested prior to bloom^a.

- Alfalfa
- Amaranth, Chinese
- Brassica leafy vegetables (Crop Group 5)
- Chervil
- Corn salad b
- Leafy vegetables (Except Brassica), Crop Group 4
- Carrot
- Lettuce
- Onion
- Parsley
- Sorrel (dock)^b
- Sugar Beet^c

^a All these crops are considered attractive to honeybees (USDA 2017) and exposure could occur if grown for seed.

^b Attractiveness is uncertain (USDA), so it is assumed attractive and exposure could occur if grown for seed.

^c Nectar only

^a All these crops are considered attractive to honeybees (USDA 2017) and exposure could occur if grown for seed.

^b Attractiveness is uncertain (USDA), so it is assumed attractive and exposure could occur if grown for seed.

^c Nectar only

Refined Tier I RQs for crops with potential exposure

As discussed in **Attachment 4**, residue data are available for pollen and nectar from several crops (*i.e.*, corn, soybean, canola and cotton) that received seed treatments. This attachment recommended refined exposure values for Tier I and II (if needed) assessments. For clothianidin, those exposure recommendations

are provided in **Table 5-7** and **Table 5-8** has the recommendations for thiamethoxam (based on the relevant crop and seed treatment rates).

Table [STYLEREf 1 \s]-7. Tier I recommendations for clothianidin residues in pollen and nectar based on measured residues in these matrices from seed treatments.

Crop	Maximum seed treatment rate (mg a.i./seed)	Matrix	Tier I (acute) Concentration (ng a.i./g)	Tier I (chronic) Concentration (ng a.i./g)
Corn	1.3	Pollen	31	8.4
		Nectar	0	0
Cotton	0.35	Pollen	0	0
		Nectar	2.1	1.2
Soybean	0.13	Pollen	8.1	4.4
		Nectar	6.1	2.3
Canola	0.018	Pollen	7.8	5.9
		Nectar	2.0	1.4
All other crops	0.1 (note: this is not the max rate for other crops)	Pollen	3.2	1.8
		Nectar	7.6	4.5

Table [STYLEREf 1 \s]-8. Tier I recommendations for thiamethoxam residues in pollen and nectar based on measured residues in these matrices from seed treatments.

Crop	Maximum seed treatment rate (mg a.i./seed)	Matrix	Tier I (acute) Concentration (ng a.i./g)	Tier I (chronic) Concentration (ng a.i./g)
Corn	1.3	Pollen	31	8.4
		Nectar	0	0
Cotton	0.33	Pollen	0	0
		Nectar	2.0	1.1
Soybean	0.16	Pollen	10.0	5.4
		Nectar	7.5	2.9
Canola	0.015	Pollen	6.5	4.9
		Nectar	1.7	1.2
All other crops (may increase)	0.1 (note: this is not the maximum rate for other crops)	Pollen	3.2	1.8
		Nectar	7.6	4.5

Tables 5-9 and **5-10** include the refined RQs for clothianidin and thiamethoxam (respectively) for adult honey bees. RQs were not generated for larvae because of their lower values relative to adults. It was assumed that adult bees would be protective of larvae. The majority of the refined RQs are below the

acute and chronic risk LOCs, suggesting low likelihood of adverse effects as a result of exposure from these seed treatments. For crops with residues that result in RQs above the LOC, a Tier II assessment is conducted below.

Table [STYLEREf 1 \s]-9. Refined RQs (for adult honey bees) for crops with potential exposure form clothianidin seed treatments.

Crop	Rate (mg a.i./seed)	Acute RQ	Chronic RQ	Pass Tier I?	Risk Conclusion
Buckwheat	0.021	0.13	0.80	Yes	LOW
Canola	0.018	0.16	1.14	No	Proceed to Tier II
Cereal grains	0.033	0.21	1.26	No	Proceed to Tier II
Corn (field)	1.27	0.08	0.22	Yes	LOW
Corn (pop)	1.27	0.08	0.22	Yes	LOW
Corn (sweet)	0.51	0.03	0.09	Yes	LOW
Corn (sweet, ID only)	1.27	0.08	0.22	Yes	LOW
Corn (unspecified)	0.51	0.03	0.09	Yes	LOW
Cotton	0.35	0.17	0.97	Yes	LOW
Legume vegetables, Crop Group 6	0.25	1.56	9.53	No	Proceed to Tier II
Millet	0.0039	0.02	0.15	Yes	LOW
Sorghum	0.064	0.40	2.44	No	Proceed to Tier II
Soybeans	0.13	0.48	1.87	No	Proceed to Tier II
Teosinte*	0.036	0.0.002	0.006	Yes	LOW

* Corn residues are used as a surrogate for this crop because it is a relative of corn.

Table [STYLEREf 1 \s]-10. Refined RQs (for adult honey bees) for crops with potential exposure form thiamethoxam seed treatments.

Crop (or group)	Rate (mg a.i./seed)	Acute RQ	Chronic RQ	Pass Tier I?	Risk conclusion
Beans	0.15	0.94	5.7	No	Proceed to Tier II
Buckwheat	0.013	0.08	0.5	Yes	LOW
Canola	0.015	0.13	0.97	Yes	LOW
Cereal grains	0.021	0.13	0.8	Yes	LOW
Corn	1.3	0.08	0.22	Yes	LOW
Cotton	0.32	0.16	0.89	Yes	LOW
Cucurbit vegetables, Crop Group 9	0.66	4.12	25.2	No	Proceed to Tier II
Legume vegetables, Crop Group 6	0.21	1.31	8.0	No	Proceed to Tier II
Lentils	0.12	0.75	4.6	No	Proceed to Tier II
Millet	0.0025	0.02	0.1	Yes	LOW
Oilseed (except canola, cotton, sunflower)	0.017	0.11	0.6	Yes	LOW
Peanuts	0.25	1.56	9.5	No	Proceed to Tier II
Peas	0.047	0.29	1.8	No	Proceed to Tier II
Sorghum	0.065	0.41	2.5	No	Proceed to Tier II
Soybeans	0.16	0.59	2.4	No	Proceed to Tier II
Sunflower	0.21	1.31	8.0	No	Proceed to Tier II

Teosinte*	0.064	0.02	0.12	Yes	LOW
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* Corn residues are used as a surrogate for this crop because it is taxonomically similar to corn.

5.1.5 Tier I Risk Characterization for Bumble bees and Other Bee Species

Consistent with the Agency's 2014 risk assessment guidance for bees, the risk assessment of registered uses of clothianidin and thiamethoxam focuses on the honey bee, *Apis mellifera*. This focus reflects three important considerations: 1) honey bees are widely recognized as the most important managed pollinator in most regions of the world from both a commercial and ecological perspective;²⁶ 2) available nectar and pollen consumption data for honey bees and three other species of non-*Apis* bees suggests that dietary exposure to honey bees is generally representative or protective of other species of bees (USEPA 2012) and 3) standardized test methods for evaluating exposure and effects of chemicals for use in a regulatory context are much more developed for honey bees compared to non-*Apis* bees (USEPA *et al.* 2014; USEPA 2012²⁷), although recent progress has been made on test method development for bumble bees²⁸. As discussed in **Section 4**, available Tier I toxicity data for bumble bees and other species of bees suggest that honey bees are of similar sensitivity as non-*Apis* species. This supports the use of Tier I RQs to represent risks to honey bees and other species of bees. There remains uncertainty in using honey bees as a surrogate for non-*Apis* bees, given that there are thousands of species of untested non-*Apis* bees, for which their sensitivities to clothianidin and thiamethoxam are unknown; however, this uncertainty exists with other taxa (e.g., birds, fish) where only a few species are tested to represent large numbers of species within the same taxa.

As mentioned previously, off-field drift of clothianidin and thiamethoxam (from foliar spray applications) is another route of exposure which can present risks to bees. Spray, drift from foliar treatments resulted in risks at greater than 1,000 feet from the field for honey bees. Given the comparable toxicities, it is reasonable to conclude exposure to non-*Apis* species off the field via spray drift would pose a risk to individual non-*Apis* species. Exposure of non-*Apis* bees to clothianidin and thiamethoxam via soil applications are not expected to result in substantial spray drift to adjacent sites. Therefore, off-field risk from soil treatments are assumed to be low. Additionally, exposure to individual bees from off-site movement of abraded seed dust during planting is noted as a potential exposure route of concern.

Additional routes of exposure are also possible for non-*Apis* bees with different life histories than hive-dwelling honeybees. Ground nesting bees, would potentially be more susceptible to exposure via soil (in addition to dietary residues) either concentrated via spray drift or on-field. Residues in leaves are also often higher than those in other parts of the plant (**Attachments 2, 3 and 4**). Consequently, a bee species

²⁶ According to Tautz, J. (2008), approximately 80% of the world's flowering plants are pollinated by insects and 85% of these by honey bees. In all, the list of flowering plants pollinated by honey bees includes 170,000 species.

²⁷ USEPA *et al.* 2012. White Paper in Support of the Proposed Risk Assessment Process for Bees. Submitted to the FIFRA Scientific Advisory Panel for Review and Comment September 11 – 14, 2012. Office of Chemical Safety and Pollution Prevention Office of Pesticide Programs Environmental Fate and Effects Division, Environmental Protection Agency, Washington DC; Environmental Assessment Directorate, Pest Management Regulatory Agency, Health Canada, Ottawa, CN; California Department of Pesticide Regulation [[HYPERLINK "http://www.regulations.gov/"](http://www.regulations.gov/) \I\documentDetail%3DDEPA-HQ-OPP-2012-0543-0004" \h]

²⁸ Compilation of results of the ICPPR non-*Apis* working group with a special focus on the bumble bee acute oral and contact toxicity ring test 2014 ICPPR Non-*Apis* Working Group. Available at: [[HYPERLINK "http://pub.jki.bund.de/index.php/JKA/article/view/5352"](http://pub.jki.bund.de/index.php/JKA/article/view/5352) \h]

utilizing the leaf (leaf-cutting bees), may also be potentially exposed to higher levels as a result of residues in plant foliage.

5.1.6 Tier I Conclusions

Multiple lines of evidence are considered at the Tier I level including whether the crop is attractive to bees (*i.e.*, provides a source of pollen and/or nectar); whether the crop may be harvested prior to bloom, and whether there are measured residues available for which to refine risk estimates based on modeled or default EECs. Foliar applications for all uses resulted in distances >1000 feet from the edge of the field that were greater than Tier I toxicity endpoints. Tier I lines of evidence are summarized in **Table 5-11**.

When considering the non-agricultural uses of thiamethoxam, summarized above in **Section 2.4** (Use Overview), use on turf and lawns and ornamental crops are considered attractive to bees. These uses will be assessed in this risk assessment. For lawns, it is assumed that blooming weeds (*e.g.*, clover, dandelions) are present on the lawns. Well maintained turf (*i.e.*, from golf courses and sod farms), which are unlikely to contain blooming weeds are considered unattractive to bees and a low risk conclusion is made for these uses. For ornamental crops, a low risk call is made for Christmas trees and non-flowering plants due to lack of attractiveness to bees. Other registered non-agricultural uses of thiamethoxam, including applications to airports, animal housing premises, commercial premises, residential areas and building perimeter treatments are considered unattractive to bees and so are considered to present a low risk to bees. Due to their unattractiveness, these other non-agricultural uses will not be considered further in the risk assessment.

Table [STYLEREf 1 \s]-11. Summary of Tier 1 results for honey bees (*Apis mellifera*) for the registered use patterns of thiamethoxam and clothianidin.

Group #	Crop Group	Appl. Method	Residue data available ¹	On field RQs >LOC for adults? ²	On field RQs >LOC for larvae? ²	Off Field Risk ^{3,4}	On Field Refined RQs >LOC	Is crop attractive ?	Risk Conclusion
1	Root and Tuber Vegetables	Foliar	Potato (C)	YES (A,C)	YES (C)	YES	YES	NO ⁵	LOW
		Soil	Potato (C)	YES (A,C)	NO	NA	YES	NO ⁵	
		Seed	None	YES (A,C)	YES (C)	NA	NA	NO ⁵	
		Foliar	Potato (C)	YES (A,C)	YES (C)	YES	YES	YES	Tier II
		Soil	Potato (C)	YES (A,C)	NO	NA	YES	YES	
		Seed	None	YES (A,C)	YES (C)	NA	NA	YES	
3	Bulb Vegetables	Seed	None	YES (A,C)	YES (C)	NA	NA	NO ⁵	LOW
4	Leafy Vegetables	Foliar	None	YES (A,C)	YES (C)	YES	NA	NO ⁵	LOW
		Soil	None	YES (A,C)	NO	NA	NA	NO ⁵	
		Seed	None	YES (A,C)	YES (C)	NA	NA	NO ⁵	
5	Brassica Leafy Vegetables	Foliar	None	YES (A,C)	YES (C)	YES	NA	NO ⁵	LOW
		Soil	None	YES (A,C)	NO	NA	NA	NO ⁵	
		Seed	None	YES (A,C)	YES (C)	NA	NA	NO ⁵	
6	Legume Vegetables	Foliar	Soybean (T)	YES (A,C)	YES (C)	YES	NA	YES ⁶	Tier II
		Seed	Soybean (T)	YES (A,C)	YES (C)	NA	YES	YES ⁶	LOW
8	Fruiting Vegetables	Foliar	Tomato (T)	YES (A,C)	YES (C)	YES	YES	NO ⁶	LOW
		Soil	Pepper (T) Tomato (T)	YES (A,C)	NO	NA	YES	NO ⁶	
		Foliar	Tomato (T)	YES (A,C)	YES (C)	YES	YES	YES ⁶	Tier II
		Soil	Pepper (T) Tomato (T)	YES (A,C)	NO	NA	YES	YES ⁶	
9	Cucurbit Vegetables	Foliar	Cucumber (T) Pumpkin (C)	YES (A,C)	YES (C)	YES	YES	YES ⁶	Tier II
		Soil	Cucumber (C&T) Melon (C) Pumpkins (C&T) Squash (C&T)	YES (A,C)	NO	NA	YES	YES ⁶	
		Seed	None	YES (A,C)	YES (C)	NA	NA	YES ⁶	LOW
		Foliar	None	YES (A,C)	YES (C)	YES	NA	YES ⁶	Tier II

10	Citrus Fruits	Soil	Oranges (C&T)	YES (A,C)	NO	NA	YES	YES ⁶	
11	Pome Fruits	Foliar	None	YES (A,C)	YES (C)	YES	NA	YES ⁶	Tier II
		Soil	None	YES (A,C)	NO	NA	NA	YES ⁶	
12	Stone Fruits	Foliar	Peaches, plums, cherries (T)	YES (A,C)	YES (C)	YES	YES	YES ⁶	Tier II
		Soil	None	YES (A,C)	NO	NA	NA	YES ⁶	
13	Berry and Small Fruit	Foliar	Cranberry (T), Blueberry, T, Strawberry, (t)	YES (A,C)	YES (C)	YES	YES	YES ⁶	Tier II
		Soil	Strawberry (T)	YES (A,C)	NO	NA	NA	YES ⁶	
14	Tree Nuts	Foliar	None	YES (A,C)	YES (C)	YES	NA	YES ⁶	Tier II
		Soil	None	YES (A,C)	NO	NA	NA	YES ⁶	
15	Cereal Grains	Foliar	None	YES (A,C)	YES (C)	YES	NA	YES	LOW
		Seed	Corn (C&T)	YES (A,C)	YES (C)	NA	YES	YES	
		Soil	Corn (C)	YES	YES	NA	No	YES	
18	Forage Fodder, Straw and Hay	Seed	None	YES (A,C)	YES (C)	NA	NA	YES ⁶	LOW
19	Herbs and Spices	Foliar	None	YES (A,C)	YES (C)	YES	NA	YES ⁶	Tier II
		Seed	None	YES (A,C)	YES (C)	NA	NA	YES ⁶	
20	Oilseed	Foliar	Cotton (C&T)	YES (A,C)	YES (C)	YES	YES	YES ⁶	Tier II
		Seed	Canola (C&T) Cotton (C&T) Sunflower (T)	YES (A,C)	YES (C)	NA	NO	YES ⁶	Low
23	Tropical and Subtropical Fruit	Foliar	None	YES (A,C)	YES (C)	YES	NA	YES ⁶	Tier II
24	Tropical and Subtropical Fruit	Foliar	None	YES (A,C)	YES (C)	YES	NA	YES ⁶	Tier II
		Soil	None	YES (A,C)	NO	NA	NA	YES ⁶	
Other	Artichoke	Foliar	None	YES (A,C)	YES (C)	YES	NA	YES ⁶	Tier II
		Soil	None	YES (A,C)	NO	NA	NA	YES ⁶	
	Peanuts	Seed	None	YES (A,C)	YES (C)	NA	NA	YES ⁶	LOW
	Tobacco	Foliar	None	YES (A,C)	YES (C)	YES	NA	NO ⁵	
	Turf (sod)	Foliar	None	YES (A,C)	YES (C)	YES	NA	NO ⁵	
	Turf (lawn)	Foliar	None	YES (A,C)	YES (C)	YES	NA	YES ⁶	Tier II
	Ornamentals	Foliar	Ornamental (T)	YES (A,C)	YES (C)	YES	NA	YES ⁶	

NA = not assessed.

¹T = thiamethoxam; C = clothianidin²A = acute, C = chronic³Evaluation of how far dietary exposure concentrations exceed toxicity values to individual adult bees. For all uses with a "Yes", the distance extends >1000 ft from the edge of the field (limit of Tier I spray drift model).⁴Off-site exposure not assessed for soil and seed treatments.

[PAGE * MERGEFORMAT]

⁵For uses where the crop is grown for food, crop (*e.g.*, roots, tubers, bulbs, leaves) is harvested prior to bloom. This limits exposure to bees on field, as the crop is not attractive to bees when not flowering.

⁶Applications made prior to bloom. Crop is attractive to honey bees and other bees (USDA 2016).

5.2 Higher Tier Analysis for Honey Bees

5.2.1 Tier II and III risk assessment for seed treatments

In cases where refined Tier I RQs exceed the LOC, **Attachment 4** provides residue concentrations for seed treatment uses that can be used in a Tier II assessment. **Tables 5-12** and **5-13** include the crop-specific exposure values (based on treatment rate and crop) for clothianidin and thiamethoxam. Both sets of exposure values are compared to the clothianidin CFS NOAEC (*i.e.*, 19 ng c.e./g). The clothianidin NOAEC is used since it is relevant to both thiamethoxam and clothianidin uses and is the lower of the two. If residues are below the clothianidin NOAEC, then there is low Tier II risk for uses of clothianidin or thiamethoxam. This is the case for all clothianidin uses and the all thiamethoxam seed treatment uses, except for clothianidin applications to turmeric seed pieces and thiamethoxam applications to cucurbits. Therefore, additional characterization is considered below for these two uses.

Table [STYLeref 1 \s]-12. Tier II seed assessment conclusions for clothianidin.

Crop	Tier II concentration (nectar equivalents in ng c.e. /g)	Above Clothianidin CFS NOAEC (19 ng c.e./g)?	Risk conclusion
Canola	1.7	No	LOW
Cereal grains	1.5	No	LOW
Legume vegetables	12	No	LOW
Sorghum	2.9	No	LOW
Soybeans	2.6	No	LOW

Table [STYLeref 1 \s]-[SEQ Table * ARABIC \s 1]3. Tier II seed assessment conclusions for thiamethoxam.

Crop (or group)	Tier II residue ng c.e./g	Above Clothianidin CFS NOAEC (19 ng c.e./g)?	Risk conclusion
Beans	6.9	No	LOW
Cucurbit vegetables	30	Yes	Proceed to characterization
Legume vegetables	9.7	No	LOW
Lentils	5.5	No	LOW
Peanuts	12	No	LOW
Peas	2.2	No	LOW
Sorghum	3.0	No	LOW
Soybeans	3.2	No	LOW
Sunflower	9.7	No	LOW

Since the estimated residue of 30 ng c.e./g for cucurbits is below the thiamethoxam NOAEC (of 44 ng c.e./g), there is uncertainty in whether there is colony level risk to bees. As discussed above, thiamethoxam residues of concern are a combination of thiamethoxam and clothianidin. Available residue studies from thiamethoxam seed treatments on corn, cotton, soybean and canola (summarized in **Attachment 4**) indicate that the composition of thiamethoxam in pollen and nectar of treated crops ranges 11-98% of the residues, with the majority of studies showing that thiamethoxam is the predominant component of the total residue (**Table 5-14**). This suggests that more weight should be

placed on the thiamethoxam CFS endpoints when evaluating risk. In addition, the estimated residue is below all levels where effects were observed at the colony level (*i.e.*, LOAECs). Therefore, the weight of evidence indicates that risks from thiamethoxam seed treatment of cucurbits represents a low risk to honey bee colonies.

Table [STYLEREf 1 \s]-14. Thiamethoxam content of total residues in pollen and nectar from seed treated crops.

Crop	Matrix	# samples with quantified thiamethoxam	Mean % thiamethoxam (range)*
Soybean	Nectar	8	69 (11-98)
Cotton	Nectar	2	20, 62
Canola	Nectar	4	93 (91-95)
Canola	Pollen	6	84 (73-92)
Corn	Pollen	133	59 (28-91)

For clothianidin, turmeric was identified as an attractive root and tuber crop species that, based on application rate and the estimated residues developed from the seed treatment residue bridging document (**Attachment 4**), there was potential on-field risk to honey bees foraging on attractive turmeric flower parts following seed treatment. A conclusion of risk for this use site was considered highly uncertain, due to the differences associated with clothianidin seed treatments for turmeric (where an entire seed piece or rhizome is treated) compared to other seed treatments where only the seed itself is treated. The seed treatment residue bridging is based solely on empirical data from treated seeds themselves. The relevancy of exposures from this application method to one where a piece of root/rhizome is treated is considered highly uncertain and exposures could be lower or higher than that predicted by the seed treatment bridging analysis.

As discussed in Section 4, there are several honey bee colony Tier II (tunnel) and Tier III (full field) studies available for clothianidin and thiamethoxam seed treatments. In the studies either no effects were observed (relative to controls) or transitory effects (in the form of increased mortality) were observed. This supports the conclusions that dietary exposures of bees to clothianidin and thiamethoxam through consumption of pollen and/or nectar of seed treated crops poses a low risk to honey bee colonies.

As discussed in the problem formulation (**Section 2**), exposure of bees to clothianidin and thiamethoxam via drift of abraded seed coat dust, is considered a route of concern. Section 4 describes many incident reports associated with seed treatments. For clothianidin and thiamethoxam, 27 and 5 bee kills, respectively were reported since 2012 following applications of treated corn seeds. All but six of these were reported prior to 2014. It is assumed that these incidents were associated with contaminated dust that lead to contact exposure of bees, or consumption of pollen and nectar from flowering plants (weeds) intercepting dust on or adjacent to the fields where corn was planted. This information indicates that transport of dust presents a risk concern for honey bees.

4.2.

4.3.

4.3.1.

4.3.2.

4.3.3.

5.2.2 Tier II and III risk assessment for foliar and soil applications

In cases where refined Tier I RQs exceed the LOC, the risk assessment proceeds to higher tiers to evaluate whether there are potential colony-level effects from honey bee exposure to the residues in pollen and nectar. The methodology for the higher tiered risk assessment that follows is described in more detail in the problem formulation above. The neonicotinoid residue bridging strategy for foliar and soil treatments to agricultural and non-agricultural use sites (**Attachments 2 and 3**, respectively) provides a comprehensive analysis of the available data on neonicotinoid residue concentrations in each crop group following foliar and/or soil treatments and evaluates whether residues may be bridged across the different active ingredients and/or crops within a crop group. Conclusions from this analysis are summarized below in each crop group section and the resulting empirical residues are compared to the CFS endpoints for clothianidin and thiamethoxam. Where data allowed for deriving reliable residue decline curves (*i.e.*, foliar applications to cotton, cucurbits and berries), Monte Carlo simulations were run and the resulting 50th, 70th, and 90th percentile residue decline curves are depicted to represent the median and higher bounds of potential exposure, compared to the colony effects endpoints. Additionally, other available lines of evidence (*e.g.* incident data) relevant to each crop group and chemical are considered. More detail on the higher tiered risk assessment methodology and residue strategy is provided in the problem formulation, (**Section 2.11**) and bridging strategy documents (**Attachments 2-3**), respectively.

5.2.2.1 Cotton

In the oilseed crop group, clothianidin and thiamethoxam are only registered for foliar applications to cotton. Neither chemical is registered for soil applications to cotton or other crops in the oilseed group. For clothianidin, the maximum single foliar application rate is 0.1 lb c.e./A, allowing two applications for a total of 0.2 lb c.e./A per season. For thiamethoxam, the single maximum foliar application rate is 0.063 (0.054 lb c.e./A) with two applications allowed per season.

According to USDA (2017), cotton does not require bee pollination, nor does it use managed pollinators. However, some beekeepers use cotton for honey production. Cotton nectar is considered attractive to honeybees, while pollen is not. Cotton is an indeterminate blooming crop and has a blooming duration of at least 6 weeks. The pattern of bloom is known as vertical flowering, whereby flowers bloom in a distinct, upward spiral among branches over time. Once bloom begins, each flower lasts only for 1 day. This differs from other crops (*e.g.*, stone fruit) where all blossoms develop and bloom at a similar time. Additionally, cotton is known to produce extra-floral nectar which may be attractive to honey bees. Whether honey bees have a preference of floral or extrafloral nectar is unknown. Therefore, this risk characterization for honey bees considers both floral nectar and extra-floral nectar, but not exposure to residues in pollen.

This section describes the lines of evidence associated with the assessment of risks of clothianidin and thiamethoxam to honey bee colonies from foliar applications to cotton. **For both chemicals, there is strong evidence indicating that foliar applications to cotton pose a risk to honey bee colonies foraging on treated fields.**

For clothianidin, measured residues in both floral and extrafloral nectar exceed both the CFS NOAEC and LOAEC. Residues of clothianidin are greater in extrafloral nectar compared to nectar. In floral nectar, residues exceed the NOAEC and LOAEC for 2 weeks, while they exceed these endpoints for 4 weeks in extrafloral nectar. When considering the estimated 50th percentile of the available data (based on the Monte Carlo analysis described previously), exposure exceeds the NOAEC for only 2 days for floral nectar but for 3.5 weeks for extra floral nectar. For the 90th percentile, floral residues exceed the NOAEC and LOAEC for approximately 1 week, while the extrafloral residues exceed for 6-7 weeks. Since cotton had a long bloom duration, and residues exceed colony level endpoints where effects were observed for days to weeks, there is opportunity for exposure of honey bees and subsequent colony level effects. When considering the available residue data, for floral nectar, residues from 2 of 5 sites exceeded colony level endpoints. This suggests that the risk associated with floral nectar may differ among fields. When considering extrafloral nectar, residues from all 5 sites exceed both the NOAEC and LOAEC, indicating that the risk associated with extrafloral nectar is similar among fields. For clothianidin, there is risk associated with both floral and extrafloral nectar exposure. The magnitude of the residues in extrafloral nectar is 410X and 220X above the NOAEC and LOAEC, respectively. Therefore, a small proportion (<1%) of a colony's nectar collected from extrafloral nectaries on treated cotton fields is sufficient to exceed both endpoints. In addition to comparisons of the residue data and the colony level endpoints, incident reports provide additional lines of evidence. For clothianidin, there are three incident reports available for honey bee mortality events that were associated with foliar applications of Belay Insecticide to cotton. The legality of the use was not determined in all three incidents, while the attribution of the incident to the clothianidin a.i. was determined to be probable. In at least two of the incidents, clothianidin was applied aerially. The lines of evidence supporting the risk conclusion for clothianidin are summarized in **Table 5-15** and discussed in more detail below.

For thiamethoxam, measured residues in both floral and extrafloral nectar exceed both the CFS NOAEC and LOAEC. Based on the available cotton residue study for thiamethoxam, the majority of the residue present in cotton nectar is thiamethoxam. Therefore, this analysis focuses on exceedances of the thiamethoxam CFS endpoints²⁹. Residues of thiamethoxam are greater in extrafloral nectar compared to nectar. In floral nectar, residues exceed the NOAEC and LOAEC for a week or less, while they exceed these endpoints for 4-5 weeks in extrafloral nectar. When considering the modeled data, the 50th percentile of the available data does not exceed the NOAEC for floral nectar; however, it exceeds for 1 week for extra floral nectar. For the 90th percentile, floral residues exceed the NOAEC and LOAEC for approximately 1 week, while the extrafloral residues exceed for 2.5-3 weeks. Since cotton has a long bloom duration and period where extrafloral nectar is available, and residues exceed colony level endpoints where effects were observed for days to weeks, there is opportunity for exposure of honey bees and subsequent colony level effects. When considering the available residue data, for floral and extrafloral nectar, residues from multiple sites exceeded colony level endpoints. This indicates that the risk associated with nectar spans multiple fields. For thiamethoxam, there is risk associated with both

²⁹ Note that this is not the case for other crops discussed below where clothianidin and thiamethoxam both represent a substantial portion of the total residue in pollen and/or nectar. In those cases, risk conclusions are based on comparisons of residues to both the clothianidin and thiamethoxam CFS endpoints.

floral and extrafloral nectar exposure. The magnitude of the residues in extrafloral nectar is 82X and 51X above the NOAEC and LOAEC, respectively. A small proportion (<2%) of a colony's nectar collected from extrafloral nectaries on treated cotton fields is sufficient to exceed both endpoints. The lines of evidence supporting the risk conclusion for thiamethoxam are summarized in **Table 5-16** and discussed in more detail below.

There is some uncertainty about the extent to which bees collect nectar from floral or extrafloral nectaries. Bees have been observed collecting nectar from extrafloral nectaries and extrafloral and floral nectar has similar properties that would suggest that both are attractive to honey bees. The uncertainty of how much bees consume from extrafloral nectar does not influence risk conclusions.

Table [STYLEREf 1 \s]-15. Lines of evidence considered in risk call for foliar applications of clothianidin to cotton.

Line of evidence		Clothianidin (Strong evidence of risk)	
Chemical specific residue data		Cotton	
Residue data for other chemicals		Not applicable*	
Measured data:	Exceedance Attribute	NOAEC (19 ug ce/g)	LOAEC (35.5 ug ce/g)
	Frequency: Number daily mean residue values > NOAEC or LOAEC	7 (FN) 28 (XFN)	5 (FN) 26 (XFN)
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	14 (FN) 28 (XFN)	14 (FN) 28 (XFN)
	Magnitude: Ratio of Max to NOAEC or LOAEC** (% of diet required to reach NOAEC or LOAEC)	7.5X (13%) (FN) 412X (0.2%) (XFN)	4.0X (25%) (FN) 220X (0.5%) (XFN)
Modeled Data: (90 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	10 (FN) 37 (XFN)	6 (FN) 32 (XFN)
	Magnitude: Ratio to Max to NOAEC or LOAEC ** (% of diet required to reach NOAEC or LOAEC)	4.4X (23%) (FN) 2227X (<0.1%) (XFN)	2.3X (43%) (FN) 1192X (0.1%) (XFN)
Modeled Data: (70 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	7 (FN) 30 (XFN)	3 (FN) 26 (XFN)
	Magnitude: Ratio to Max to NOAEC or LOAEC ** (% of diet required to reach NOAEC or LOAEC)	2.9X (34%) (FN) 398X (0.3%) (XFN)	1.6X (64%) 213X (0.5%) (XFN)
Modeled Data: (50 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	5 (FN) 25 (XFN)	1 (FN) 22 (XFN)
	Magnitude: Ratio to Max to NOAEC or LOAEC** (% of diet required to reach NOAEC or LOAEC)	2.0X (50%) (FN) 154X (0.6%) (XFN)	1.1X (94%) (FN) 83X (1.2%) (XFN)
Tier III data		None	
Crop Attractiveness*** & Bloom Duration		Attractive (floral nectar); Potentially attractive (extrafloral nectar); Not attractive (pollen); Long bloom duration (indeterminant bloom)	
Managed pollinators***		Not Required, but cotton used for honey production by some commercial beekeepers	
Ecological incidents		Three reports involving honey bee kills following foliar applications to cotton	
Spatial extent of risk (annual acres treated)		<192,000 (average and maximum)	
Other Considerations		The extent to which bees collect nectar from extrafloral nectaries is unknown. Floral nectar residues from 2 of 5 sites exceed both the NOEC and the LOAEC. Extrafloral nectar residues exceed both the NOAEC and LOAEC from all 5 sites.	

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FN = floral nectar, XFN = extrafloral nectar, N.C. = not calculated because > 100% of the treated diet would be needed to reach the NOAEC

*Chemical specific residues were used. The available clothianidin data were sufficient to characterize the magnitude of clothianidin in nectar over time.

**Maximum measured value represents 1 day after application for floral nectar and 6 days for extrafloral nectar. Maximum modeled value represents 1 day after application for both floral and extrafloral nectar.

***Based on USDA 2017

Table [STYLEREf 1 \s]-16. Lines of evidence considered in risk call for foliar applications of thiamethoxam to cotton.

Line of evidence		Thiamethoxam (Strong evidence of risk)			
Chemical specific residue data		Cotton			
Residue data for other chemicals		Clothianidin, Dinotefuran, and imidacloprid			
Percent of clothianidin present in residues from thiamethoxam studies		Median: 3%; Mean: 4%; Range: 1-23%			
Measured data:	Exceedance Attribute	Clothi NOAEC (19 ug ce/g)	Clothi LOAEC (35.5 ug ce/g)	Thia NOAEC (44 ug ce/g)	Thia LOAEC (81 ug ce/g)
	Frequency: Number daily mean residue values > NOAEC or LOAEC	19 (FN) 47 (XFN)	9 (FN) 40 (XFN)	6 (FN) 38 (XFN)	3 (FN) 29 (XFN)
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	14 (FN) 28 (XFN)	9 (FN) 25 (XFN)	7 (FN) 25 (XFN)	6 (FN) 21 (XFN)
	Magnitude: Ratio of Max to NOAEC or LOAEC* (% of diet required to reach NOAEC or LOAEC)	5.0x (20%) (FN) 218x (0.46%) (XFN)	2.7x (37%) (FN) 117x (0.9%) (XFN)	2.1x (48%) (FN) 82x (1.1%) (XFN)	1.2x (83%) (FN) 51x (2.0%) (XFN)
Modeled Data: (90 th percentile)	Duration: Number of days > NOAEC & LOAEC	10 (FN) 30 (XFN)	8 (FN) 24 (XFN)	7 (FN) 23 (XFN)	6 (FN) 18 (XFN)
	Magnitude: Ratio to Max to NOAEC & LOAEC* (% of diet required to reach NOAEC & LOAEC)	20.4x (4.9%) (FN) 369x (0.3%) (XFN)	10.9x (9.2%) (FN) 198 (0.5%) (XFN)	8.8x (11.4%) (FN) 159x (0.6%)(XFN)	4.8x (20.9%) (FN) 87x (1.2%) (XFN)
Modeled Data: (70 th percentile)	Duration: Number of days > NOAEC & LOAEC	7 (FN) 22 (XFN)	4 (FN) 18 (XFN)	2 (FN) 16 (XFN)	0 (FN) 13 (XFN)
	Magnitude: Ratio to Max to NOAEC & LOAEC* (% of diet required to reach NOAEC & LOAEC)	3.2X (31%) (FN) 55X (1.8%) (XFN)	1.7X (58%) (FN) 30X (3.4%) (XFN)	1.4X (72%) (FN) 24X (4.2%) (XFN)	0.8X (NC) (FN) 13x (7.7%) (XFN)
Modeled Data: (50 th percentile)	Duration: Number of days > NOAEC & LOAEC	3 (FN) 18 (XFN)	0 (FN) 14 (XFN)	0 (FN) 13 (XFN)	0 (FN) 10 (XFN)
	Magnitude: Ratio to Max to NOAEC & LOAEC* (% of diet required to reach NOAEC & LOAEC)	1.5x (NC) (FN) 22x (4.5%) (XFN)	<1x (NC) (FN) 12x (8.5%) (XFN)	<1x (NC) (FN) 9.5x (11%) (XFN)	<1x (NC) (FN) 5.21x (19%) (XFN)
Tier III data		None			

Line of evidence	Thiamethoxam (Strong evidence of risk)
Crop Attractiveness** & Bloom Duration	Attractive (floral nectar); Potentially attractive (extrafloral nectar); Not attractive (pollen); Long bloom duration (indeterminant bloom)
Managed pollinators**	Not Required, but cotton used for honey production by some commercial beekeepers
Ecological incidents	None
Spatial extent of risk (annual acres treated)	766,000 (average) 1,150,000 (maximum)
Other Considerations	The extent to which bees collect nectar from extrafloral nectaries is unknown. Residue data are bridged from all 4 neonicotinoids. Note that none of the thia data exceed thia endpoints for FN.

FN = floral nectar, XFN = extrafloral nectar, N.C. = not calculated because > 100% of the treated diet would be needed to reach the NOAEC

*Maximum measured value represents 1 day after application for floral nectar and 6 days for extrafloral nectar. Maximum modeled value represents 1 day after application for both floral and extrafloral nectar. **Based on USDA 2017

The risk conclusions are based on field level exposures to individual colonies. According to USDA 2017 there were approximately 7.7 million acres of cotton planted (ELS and Upland) in 2017. When considering estimated annual usage on cotton, 10,000 lbs of clothianidin and 60,000 lbs of thiamethoxam are applied each year via foliar application (**Table 5-17**). When considering percent crop treated data provided by BEAD in combination with the acres of cotton grown in the US, the spatial extent of risk of clothianidin is <192,000 acres per year for clothianidin and 766,000 acres per year for thiamethoxam (on average). On a year with higher usage, 1.15 million acres may be treated with thiamethoxam on a given year.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]7. Usage data for foliar and soil applications of clothianidin and thiamethoxam to cotton.

Chemical	Lbs. Applied (per year)	Percent Crop Treated (per year)*		Acres treated (per year)**	
		Average	Maximum	Average	Maximum
Clothianidin	10,000	<2.5	<2.5	<192,000	<192,000
Thiamethoxam	60,000	10	15	766,000	1,150,000

*From SLUA

**Calculated by multiplying acres grown (7.7 mil A) of cotton by PCT.

Clothianidin

The residue bridging analysis for foliar applications to cotton (**Attachment 2**) examined whether residues were comparable across the different neonicotinoid compounds for generating reliable residue dissipation curves. The analysis for cotton indicated difference in the dissipation rates of clothianidin and imidacloprid. Therefore, the tier II analysis for clothianidin is based on the available clothianidin residue studies-alone for cotton. These data are from two different studies that cover 5 locations (in MO, TX and CA; MRIDs 49904901 and 49733302). Residue data for MRID 49904901 include trials of a single foliar application either alone or following seed treatment (applications separated by approximately 70 days). Based on residue data for the seed treatment alone (same study), the seed treatment itself added minimal residues to the overall exposure. Therefore, both the single foliar application and the combined seed + foliar application were included in this analysis. MRID 49733302 included residues following two foliar applications (to sites in CA). The available clothianidin data regarding the distribution of dissipation rate constants and concentrations of total clothianidin (normalized to day 15) were sufficient to be used in a Monte Carlo analysis to describe the upper 50th, 70th, and 90th percentiles of residue decline curves in cotton floral and extra-floral nectar.

For floral nectar, the residue decline curves are shown in relation to the measured residues of clothianidin (**Figure 5-1**). Residue values were normalized to the total maximum foliar application rate of 0.2 lb c.e./A. With floral nectar, empirical mean measured residues of total clothianidin generally remain above the colony-level NOAEC of 19 µg c.e./kg and LOAEC of 35.5 µg c.e./kg for at least 14 days after the last application. Based on the Monte Carlo analysis of clothianidin residues and associated kinetic parameters, the predicted exceedance of the NOAEC range from 5 days (50th percentile) to 10 days (90th percentile; **Table 5-15**). At the maximum daily mean residue of 142 µg c.e./kg, cotton floral nectar would have to represent >13.4% of the diet of a honey bee colony to exceed the NOAEC. When considering the available residue data, floral nectar concentrations from 2 of the 5 sites exceed the NOAEC and LOAEC for clothianidin. Both of the sites were located in California (MRID 49733302).

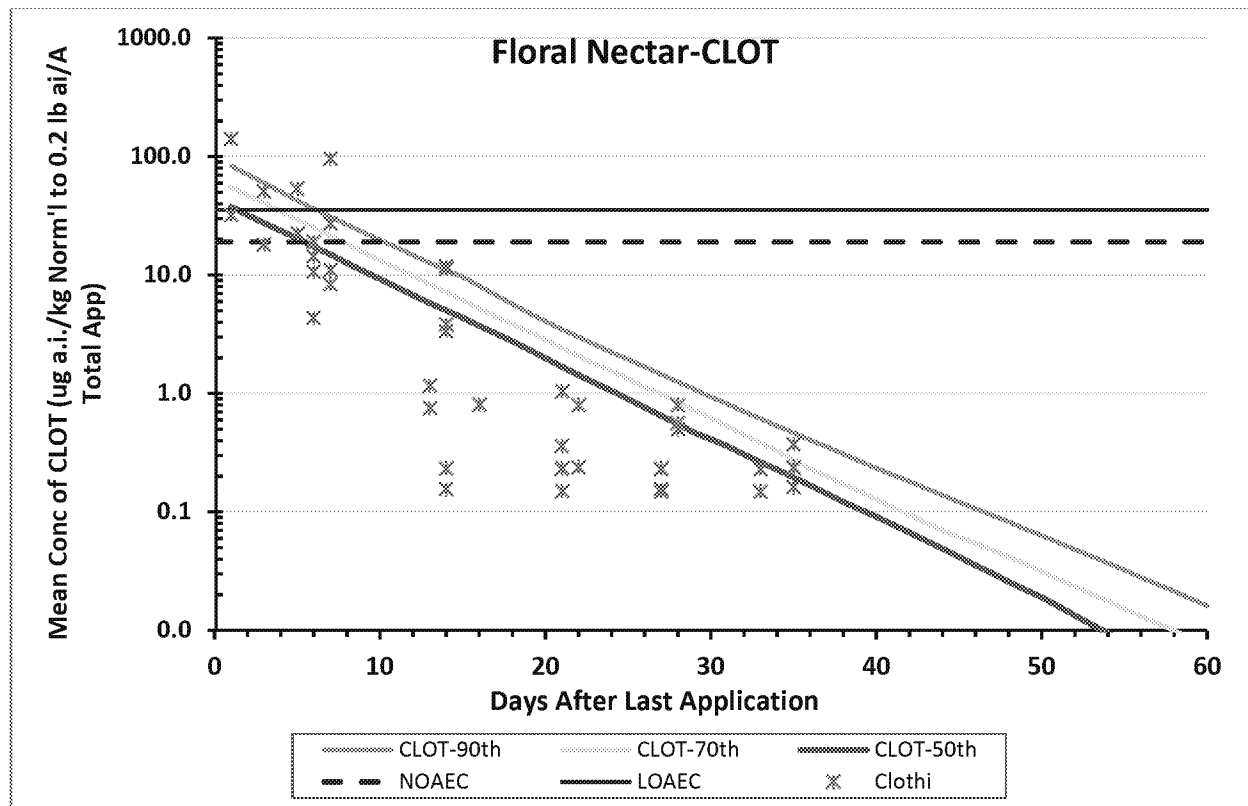


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]. Mean concentration (+/- 95% CL) of total clothianidin in cotton floral nectar (adjusted to the maximum seasonal foliar rate of 0.2 lb c.e./A) following either a single foliar or seed + one foliar application in 3 trials in California, Missouri and Texas (MRID 49904901) or two foliar applications in 2 trials in California (MRID 49733302). Dashed and solid horizontal lines represent the honey bee colony-level NOAEC (19 ng c.e./g-sucrose) and LOAEC (35.5 ng c.e./g-sucrose) in, respectively. Orange, yellow and blue curves represent the upper 90th, 70th and 50th percentiles from the Monte Carlo analysis of residue decline kinetics (Attachment 2).

Measured residues in extra-floral nectar exceed the NOAEC and LOAEC for 28 and 26 days, respectively. (Figure 5-2). At the maximum daily mean residues of 7823 µg c.e./kg extra-floral nectar would have to represent only <1% of the diet to exceed the colony-level NOAEC. Based on the Monte Carlo analysis of clothianidin residues and associated kinetic parameters, the predicted exceedance of the NOAEC range from 25 days (50th percentile) to 37 days (90th percentile; Table 5-15). When considering the LOAEC, the Monte Carlo analysis estimated residues are estimated to exceed from 22 days (50th percentile) to 32 days (90th percentile; Table 5-15). When considering the available residue data, extrafloral floral nectar concentrations from all 5 of the sites exceed the NOAEC and LOAEC for clothianidin.

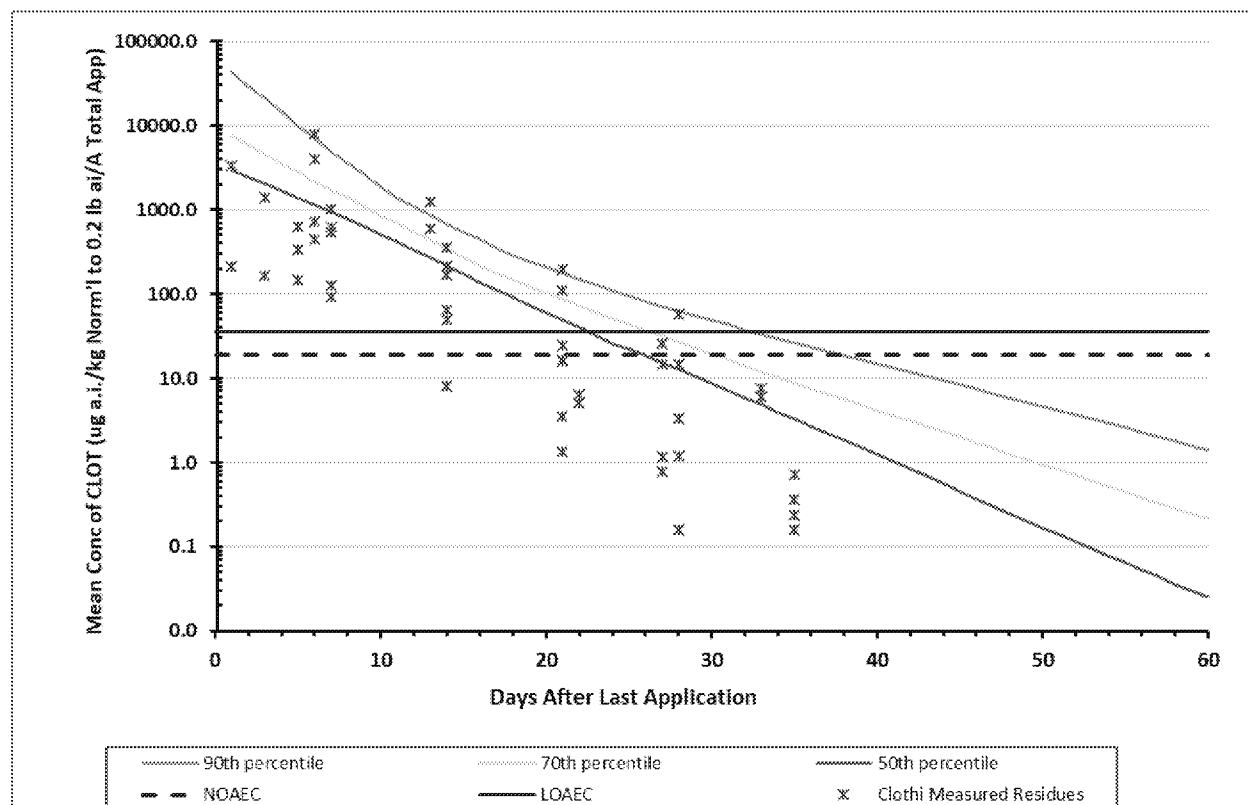


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]. Mean concentration (+/- 95% CL) of total clothianidin in cotton extrafloral nectar (adjusted to the maximum seasonal foliar rate of 0.2 lb c.e./A) following either a single foliar or a seed + one foliar application in 3 trials in California, Missouri and Texas (MRID 49904901) or two foliar applications in 2 trials in California (MRID 49733302). Dashed and solid horizontal lines represent the honey bee colony-level NOAEC (19 ng c.e./g -sucrose) and LOAEC (35.5 ng c.e./g -sucrose) in, respectively. Orange, yellow and blue curves represent the upper 90th, 70th and 50th percentiles from the Monte Carlo analysis of residue decline kinetics (Attachment 2).

Thiamethoxam

One residue study is available for thiamethoxam applications to cotton grown in California (MRID 49686801). Because this study only included one sampling period per site per year, the dissipation of total thiamethoxam residues could not be quantified. Therefore, residues from all available cotton studies for imidacloprid (MRID 49511702), clothianidin (MRIDs 49904901 and 49733302) and dinotefuran (MRID 50198501) were used to estimate the 50th, 70th and 90th percentile residues over time (using a Monte Carlo analysis). As discussed above (for clothianidin) the bridging analysis indicated a difference in the dissipation rates of clothianidin and imidacloprid in cotton nectar, leading to the decision above to use only clothianidin residue data to represent exposure from clothianidin applications. In this case, thiamethoxam data are insufficient to represent residues over time due to a lack of data. The bridging analysis indicated that “residues in floral nectar and extrafloral nectar are comparable up through 20 and 35 DALA, respectively” for the available chemicals. Since the residues are below the thiamethoxam and clothianidin CFS endpoints before 20 and 35 DALA, for floral and extrafloral nectar (respectively), the difference observed in clothianidin and imidacloprid does not influence the thiamethoxam assessment.

Additional details on this approach and the available studies is provided in **Attachment 2**.

As discussed previously, thiamethoxam is transformed to clothianidin within plants. When considering the available thiamethoxam residue study for cotton (MRID 49686801), clothianidin was not detected in floral nectar data. For extrafloral nectar, clothianidin was detected in 47% of individual samples. When both thiamethoxam and clothianidin were quantified in samples, clothianidin represented 1-23% of the residues, with a median of 3% and an average of 4%. This suggests that for exposure to bees from cotton nectar, thiamethoxam is the predominant portion of the residues of concern. Therefore, greater emphasis is placed here on the thiamethoxam colony level endpoints (*i.e.*, NOAEC of 44 and LOAEC of 81 ng c.e./g).

For floral nectar, the residue decline curves are shown in relation to the measured residues of all available neonicotinoids (**Figure 5-3**). Residues are only depicted out to 20 DALA, based on recommendations of the bridging strategy. Residue values were normalized to the total maximum foliar application rate of 0.11 lb c.e./A. Empirical residues exceed the thiamethoxam NOAEC and LOAEC for 7 and 6 d (respectively). Based on the Monte Carlo analysis of thiamethoxam residues and associated kinetic parameters, the predicted exceedance of the NOAEC range from 0 days (50th percentile) to 7 days (90th percentile; **Table 5-16**). For the thiamethoxam LOAEC, estimated residues exceed from 0 d (50th percentile) to 6 d (90th percentile). When considering the available residue data, floral nectar concentrations from multiple sites exceed the NOAEC and LOAEC thiamethoxam. It should be noted that none of the residues from the thiamethoxam study exceed the CFS endpoints.

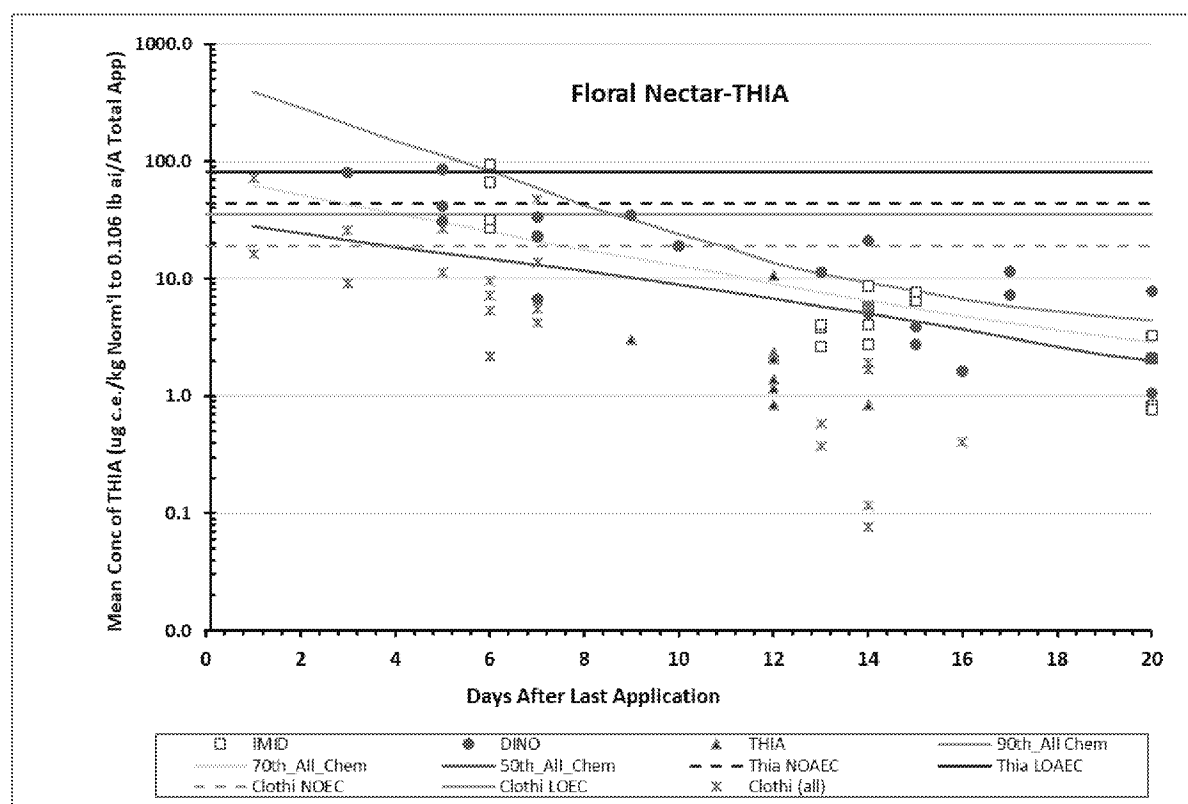


Figure [STYLEREf 1 \s].[SEQ Figure * ARABIC \s 1]. Mean concentration of thiamethoxam (in c.e.) and other neonicotinoids in cotton floral nectar (adjusted to the maximum seasonal foliar rate of 0.11 lb c.e./A) from trials conducted in California. Orange, yellow and blue curves represent the 90th, 70th, and 50th percentiles from the Monte Carlo analysis of residue decline kinetics (Attachment 2) using data from all neonicotinoids. Dashed and solid horizontal lines represent the honey bee colony-level NOAEC and LOAEC, respectively for thiamethoxam and clothianidin.

For extrafloral nectar, daily empirical mean measured residues of neonicotinoids exceed the thiamethoxam CFS NOAEC and LOAEC for 3 weeks or more (**Figure 5-4**). At the maximum daily mean residues of 4146 $\mu\text{g c.e./kg}$ extra-floral nectar would have to represent >1.1% of the diet to exceed the colony-level NOAEC. The days with measured residues exceeding the NOAEC and LOAEC for extra-floral nectar is 25 and 21, respectively. When considering the available residue data, extrafloral floral nectar concentrations from multiple sites exceed the NOAEC and LOAEC for thiamethoxam. Based on the Monte Carlo analysis of neonicotinoid residues and associated kinetic parameters, the predicted exceedance of the thiamethoxam NOAEC range from 13 days (50th percentile) to 23 days (90th percentile; **Table 5-16**). For the thiamethoxam LOAEC, estimated residues exceed from 10 d (50th percentile) to 18 d (90th percentile).

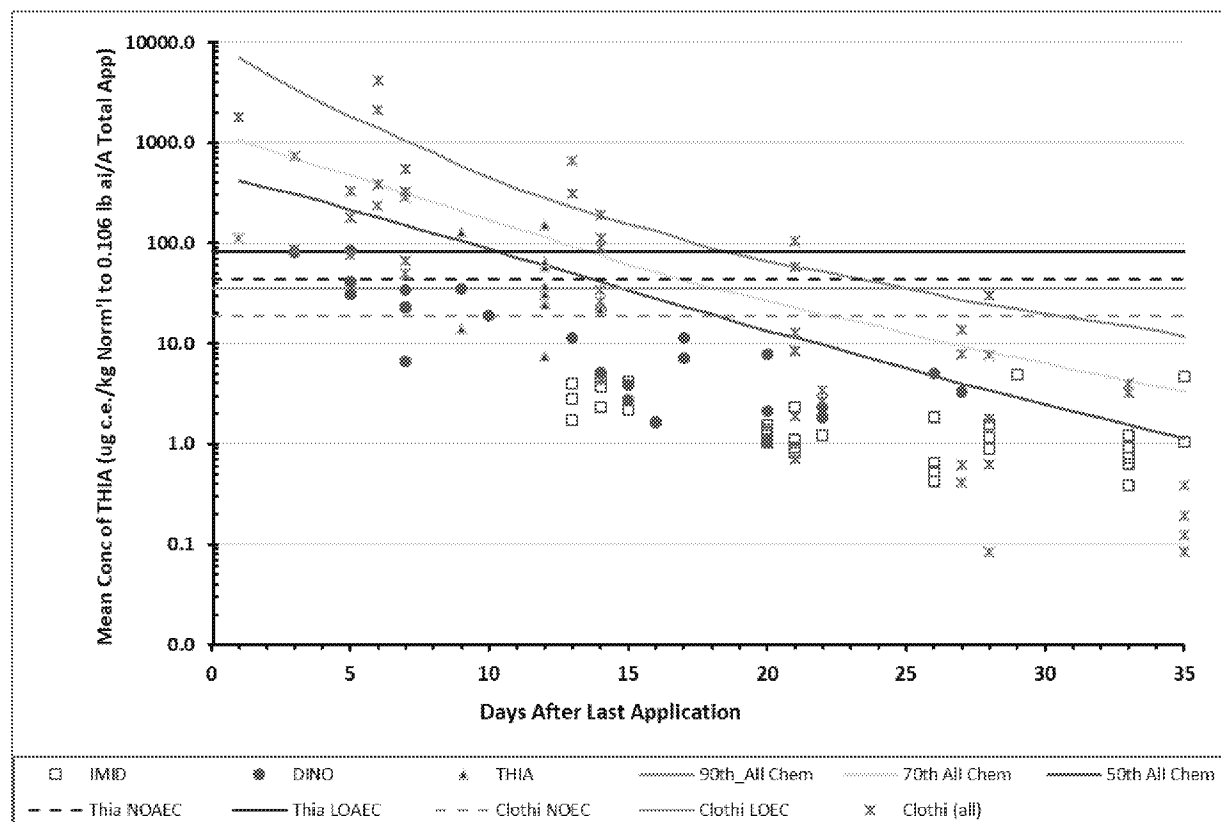


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]. Mean concentration of thiamethoxam (in c.e.) and other neonicotinoids in cotton extrafloral nectar (adjusted to the maximum seasonal foliar rate of 0.11 lb c.e./A). Orange, yellow and blue curves represent the 90th, 70th, and 50th percentiles from the Monte Carlo analysis of residue decline kinetics (Attachment 2) using data from all neonicotinoids. Dashed and solid horizontal lines represent the honey bee colony-level NOAEC and LOAEC, respectively for thiamethoxam and clothianidin.

5.2.2.2 Cucurbit Vegetables

Both clothianidin and thiamethoxam are registered for foliar and soil applications to cucurbits. Clothianidin is registered for two foliar applications at 0.1 lb c.e./A each and a single application to soil at a rate of 0.2 lb c.e./A. Thiamethoxam is registered for two foliar applications of 0.075 lb c.e./A and 1 soil application of 0.15 lb c.e./A (clothianidin equivalents). Estimated annual usage of clothianidin and thiamethoxam are summarized in **Table 5-17**. These data indicate that <2500 lbs clothianidin and <3000 lbs of thiamethoxam are applied per year to cucurbit crops. Of all cucurbit crops, the greatest amount of thiamethoxam applied per year is to cantaloupe (1,000 lbs/year). Based on the available usage data, cantaloupe represents the largest percent crop treated per year, with an average of 5% and a maximum of 25% of crop acres treated.

Table [STYLEREf 1 \s]-17. Estimated annual usage of clothianidin and thiamethoxam on cucurbit crops (foliar and soil applications; source: SLUAs)—Reporting Time 2005-2014.

Cucurbits crop	Clothianidin	Thiamethoxam
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	Estimated lbs applied/year (based on SLUA)	PCT (annual average)	PCT (annual max)	Estimated lbs applied/year (based on SLUA)	PCT (annual average)	PCT (annual max)
Cantaloupe	<500	<2.5	<2.5	1000	5	25
Cucumber	<500	<1	<2.5	<500	5	10
Pumpkins	<500	<2.5	<2.5	<500	<2.5	10
Squash	<500	<2.5	<2.5	<500	5	10
Watermelon	<500	<2.5	<2.5	<500	5	10

According to USDA (2017), both pollen and nectar of cucurbit crops (including cucumbers, pumpkins, squash, gourds, and watermelons) are attractive to honey bees. In addition, these crops require and utilize managed pollinators. Therefore, the assessment for cucurbits considers exposures from both pollen and nectar.

This section describes the lines of evidence associated with the assessment of risks of clothianidin and thiamethoxam to honey bee colonies from foliar and soil applications to cucurbits. **For both chemicals, a robust weight of evidence (*i.e.* strong weight) indicates that foliar application to cucurbits pose a risk to honey bee colonies foraging on treated fields. For soil applications, the lines of evidence are not as strong as for the foliar risk conclusions, resulting in a risk call with moderate weight of evidence for clothianidin soil treatments, and only weak confidence in the conclusion of risk from thiamethoxam soil treatments.**

For clothianidin, these lines of evidence include that both empirical and estimated residues in nectar and pollen (expressed as total nectar equivalents) exceed colony level NOAEC and LOAEC values for periods of time that range from days to weeks. Given the magnitude of empirical neonicotinoid residues at the maximum daily mean measurement (296 ng c.e./g) for foliar applications, only 6.4% and 12% of a colony's diet in terms of total nectar equivalents collected from flowers on treated cucurbit fields would be required to exceed the clothianidin colony level NOAEC and LOAEC, respectively. Similarly, but to a lesser extent, using the magnitude of empirical residues at the maximum measurement for soil applications (40 ng c.e./g) would necessitate 47.6% and 88.9% of a colony's diet in terms of total nectar equivalents collected from flowers from treated cucurbit fields is required to exceed the clothianidin colony level NOAEC and LOAEC, respectively. For foliar data, although clothianidin-only residues were below the colony level NOAEC endpoints, it is notable that other measured neonicotinoid residues exceed the clothianidin colony level endpoints for multiple crops, locations and sampling times, and that the clothianidin data were limited to pumpkin, a crop which appeared to have lower neonicotinoid residues than other tested cucurbit crops for the other neonicotinoids (*e.g.* thiamethoxam). As a result, for foliar applications of clothianidin to cucurbits, there is strong evidence of risk. The comparatively decreased confidence in the risk call for clothianidin soil applications (moderate weight of evidence) is due to relatively few measurements above the colony effect endpoints (considering the overall number of residue samples available for the cucurbit crop group) with at most 1-2 sites/crop having residues that exceed the colony level endpoints (suggesting that risk may be influenced by site).

Similar to the clothianidin risk conclusions, for foliar applied thiamethoxam, when using the empirical residues at the maximum daily mean measurement of 222 ng c.e./g, 20% and 36.5% of a colony's diet in terms of total nectar equivalents collected from flowers on treated cucurbit fields would be required to exceed the thiamethoxam colony level NOAEC and LOAEC, respectively. In contrast to the clothianidin soil risk assessment and both the clothianidin and thiamethoxam foliar risk assessments, for

thiamethoxam soil applications, >100% of a colony's diet in terms of total nectar equivalents would have to be acquired from the treated cucurbit field to exceed the thiamethoxam colony level NOAEC and 63.4% of a colony's diet in terms of total nectar equivalents collected from the treated field would exceed the clothianidin colony level NOAEC, suggesting that dilution of concentrations from other sources may have substantial influence on the risk conclusion for thiamethoxam soil uses. As such, more lines of evidence support the conclusion that the clothianidin soil and foliar applications and the thiamethoxam foliar applications pose a risk, than for the thiamethoxam soil application. However, a recent incident report (2018) for bees following soil application of thiamethoxam to watermelon provides an additional line of evidence for potential colony-level risks of thiamethoxam soil applications. **Tables 5-18** and **5-19** summarizes the details of the lines of evidence supporting the risk conclusions for foliar and soil applications of these chemicals to cucurbits.

Table [STYLEREf 1 \s]-18. Lines of evidence considered in risk call for foliar and soil applications of clothianidin to cucurbits.

Line of evidence		Clothianidin, Foliar (Strongest Evidence of Risk)		Clothianidin, Soil (Moderate Evidence of Risk)	
Chemical specific residue data		Pumpkin		Pumpkin, cucumber, cantaloupe, squash	
Residue data for other chemicals		Thiamethoxam (pumpkin, cucumber), Imidacloprid (watermelon)		Thiamethoxam (Pumpkin, Cucumber, muskmelon, squash), dinotefuran (Pumpkin) imidacloprid (watermelon, melon)	
Exposure	Exceedance Attribute	NOAEC (19 µg ce/g)	LOAEC (35.5 µg ce/g)	NOAEC (19 µg ce/g)	LOAEC (35.5 µg ce/g)
Measured Data (all neonics)	Frequency: Number daily mean residue values > NOAEC & LOAEC	15	12	11	4
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	19	19	57	47
	Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	15.6x (6.4%)	8.3x (12.0%)	2.1x (47.6%)	1.1x (88.9%)
Measured data (clothianidin)	Frequency: Number daily mean residue values > NOAEC & LOAEC	0	0	2	0
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	N/A	N/A	37	0
	Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	>100%	>100%	1.8x (55.4%)	0.97x (103.5%)
Modeled Data: (90 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	23	14	Not applicable	
	Magnitude: Ratio to Max to NOAEC & LOAEC ⁽²⁾ (% of diet required to reach NOAEC & LOAEC)	15.8x (6.3%)	8.4x (11.8%)		
Modeled Data (70 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	15	10		

Line of evidence		Clothianidin, Foliar (Strongest Evidence of Risk)		Clothianidin, Soil (Moderate Evidence of Risk)
	Magnitude: Ratio to Max to NOAEC & LOAEC ⁽²⁾ (% of diet required to reach NOAEC & LOAEC)	6.4x (15.7%)	3.4x (29.4%)	
Modeled Data: (50 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	12	7	
	Magnitude: Ratio to Max to NOAEC & LOAEC ⁽²⁾ (% of diet required to reach NOAEC & LOAEC)	3.8x (26.2%)	2.0x (49.0%)	
Crop Attractiveness* & Bloom Duration		Highly attractive (nectar and pollen); long bloom duration (Indeterminate bloom)		
Managed Pollinators		Required		
Ecological incident reports		None		
Spatial extent of risk (annual acres treated)		Cucumbers: <1,200 (ave), <3,100 (max) Pumpkins: <1,100 (ave and max) Squash: <1,100 (ave and max) Watermelons: <3,100 (ave and max)		
Other considerations		Some cucurbit crops (cucumber) appear to have higher residues than others (pumpkin). Only pumpkin data are available for clothianidin.		Residues for 1-2 sites exceed colony level endpoints.

*Based on USDA 2018

¹ Maximum measured mean value was for samples taken 5 days or 35 days after last application for foliar and soil applications, respectively.² Maximum modeled value is for 1 day after last application

Table [STYLEREf 1 \s]-19. Lines of evidence considered in risk call for foliar and soil applications of thiamethoxam to cucurbits.

Line of evidence	Thiamethoxam, Foliar (Strongest Evidence of Risk)	Thiamethoxam, Soil (Moderate Evidence of Risk)
Chemical specific residue data	Pumpkin, cucumber	Pumpkin, cucumber, cantaloupe, squash
Residue data for other chemicals	Clothianidin (pumpkin), Imidacloprid (watermelon)	Thiamethoxam (Pumpkin, Cucumber, muskmelon, squash), dinotefuran (Pumpkin) imidacloprid (watermelon, melon)

Line of evidence		Thiamethoxam, Foliar (Strongest Evidence of Risk)				Thiamethoxam, Soil (Moderate Evidence of Risk)			
Percent of clothianidin present in residues (average)		Cucumber: 8% (nectar), 12% (pollen) Pumpkin: 14% (nectar), 43% (pollen)				Muskmelon: 22% (nectar), 48% (pollen) Pumpkin: 29% (nectar), 48% (pollen) Squash: 18% (nectar), 33% (pollen)			
Exposure	Exceedance Attribute	Clothi NOAEC	Clothi LOAEC	Thia NOAEC	Thia LOAEC	Clothi NOAEC	Clothi LOAEC	Thia NOAEC	Thia LOAEC
Measured Data (all neonics)	Frequency: Number daily mean residue values > NOAEC & LOAEC	14	8	8	5	7	0	0	0
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	19	19	16	15	57	0	0	0
	Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	11.7x (8.6%)	6.3x (16.0%)	5.0x (19.8%)	2.7x (36.5%)	1.6x (63.4%)	0.8x (119%)	0.7x (147%)	0.4x (270%)
Measured data (thiamethoxam)	Frequency: Number daily mean residue values > NOAEC & LOAEC	14	8	8	5	6	0	0	0
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	19	19	16	15	57	0	0	0
	Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	11.7x (8.6%)	6.3x (16.0%)	5.0x (19.8%)	2.7x (36.5%)	1.6x (63.4%)	0.8x (119%)	0.7x (147%)	0.4x (270%)

Line of evidence		Thiamethoxam, Foliar (Strongest Evidence of Risk)				Thiamethoxam, Soil (Moderate Evidence of Risk)
Modeled Data: (90 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	19	11	9	5	Not applicable
	Magnitude: Ratio to Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	11.8x (8.4%)	6.3x (15.8%)	5.1x (19.6%)	2.8x (36.0%)	
Modeled Data (70 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	13	8	6	1	
	Magnitude: Ratio to Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	4.8x (21.0%)	2.5x (39.2%)	2.1x (48.6%)	1.1x (89.5%)	
Modeled Data: (50 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	10	5	3	0	
	Magnitude: Ratio to Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	2.9x (35.0%)	1.5x (65.4%)	1.2x (81.0%)	0.7x (>100%)	
Crop Attractiveness ⁽²⁾ & Bloom Duration		Highly attractive (nectar and pollen); long bloom duration (Indeterminate bloom)				

Line of evidence	Thiamethoxam, Foliar (Strongest Evidence of Risk)	Thiamethoxam, Soil (Moderate Evidence of Risk)
Managed Pollinators	Required	
Tier II or III Data	A tier II (tunnel) study is available for foliar applications of thiamethoxam to melons (at 0.089 lb a.i./A, which is above the single maximum rate of 0.075 lb a.i./A, but below the maximum total rate of 0.15 lb a.i./A). Increased mortality of adult bees was observed in bees exposed 5 and 10 d after the application (i.e., 5 and 10 days before bloom). Flight intensity also decreased in exposed bees.	A field study is available for bees exposed following soil applications (at 0.18 lb a.i./A, which is comparable to the max rate of 0.15 lb a.i./A) to honey dew melons, made 1 and 33 days before flowering. An increase in mortality was observed in applications made 1 day before flowering; while no significant effect was observed for the application made 33 d before exposure.
Ecological incident reports	None	One incident was recently reported (2018) where a bee kill occurred after an application of thiamethoxam to watermelons (in CA). Residues of thiamethoxam were detected on dead bees.
Spatial extent of risk (annual acres treated)	Cucumbers: 6,100 (ave), 12,000 (max) Pumpkins: <1,100 (ave), 4,600 (max) Squash: 2,300 (ave), 4,600 (max) Watermelons: 6,200 (ave), 12,000 (max)	
Other considerations	Some cucurbit crops (cucumber) appear to have higher residues than others (pumpkin).	Residues for 1-2 sites exceed colony level endpoints.

*Based on USDA 2017

¹ Maximum measured mean value was for samples taken 5 days or 35 days after last application for foliar and soil applications, respectively.

² Maximum modeled value is for 1 day after last application

The risk conclusion is based on field level exposures to individual colonies. When considering percent crop treated data provided by BEAD in combination with the acres of cucurbits grown in the US, the spatial extent of risk is <6500 acres per year for clothianidin and 14,600-15,700 acres per year for thiamethoxam (on average). On a year with higher usage, 33,200 acres may be treated with thiamethoxam on a given year.

Clothianidin: **Foliar applications**

The results of the bridging analysis for foliar applications to cucurbits (**Attachment 2**) concludes that overall residues in pollen and nectar for different cucurbit crops and neonicotinoids can be used to represent all cucurbit crops in the group and all four chemicals, despite some observed intra-crop differences (*e.g.* thiamethoxam residues in pumpkin compared to cucumber). There are two studies that examine residue concentrations in nectar and pollen following foliar-applied clothianidin to pumpkins (MRIDs 49602802 and 49910601). Based on the bridging analysis (**Attachment 2**), cucurbit data from thiamethoxam (MRIDs 49804105 and 50265506) and imidacloprid (MRID 50357101) applications to pumpkin, melon, squash and/or cucumber can be used to assess exposure to honey bees. For foliar applications, the residue bridging analyses (**Attachment 2**) suggest that crop may have an influence on residue concentrations, whereas the chemical does not have an influence. This is primarily based on similar concentrations across chemical and matrix (*e.g.*, pollen and nectar) for clothianidin and thiamethoxam residues in pumpkin while thiamethoxam residues in nectar and pollen of cucumbers appeared to be consistently higher than thiamethoxam residues in nectar and pollen of pumpkins.

Using the available residue data, distributions for the cucurbit crop group were developed to estimate the 50th, 70th, and 90th percentile residues over time (using a Monte Carlo analysis). Measured residue data and the associated 50th and 90th percentiles are presented in **Figure 5-5**, along with the NOAEC and LOAEC endpoints from the available clothianidin CFS study. Residue concentrations were normalized to the maximum total (seasonal) application rate registered across the cucurbit crop group (*i.e.*, 0.2 lb c.e./A). Predicted residue concentrations based on the 50th and 90th percentile curves exceed the NOAEC of 19 ng c.e./g. Mean-measured residues (normalized to total application rate) from foliar applications of neonicotinoids to cucurbit crops range from 0.1 to 296 ng c.e./g, with 15 (22%) and 12 (18%) of values above the clothianidin CFS NOAEC and LOAEC, respectively. Measured concentrations exceeding the NOAEC and LOAEC persist for up to 20 days after application while the 90th percentile Monte Carlo data distribution exceeds the NOAEC for up to 23 days after application and the LOAEC for up to 14 days after application. At the maximum measured application-normalized concentration of 296 ng c.e./g, honey bee colonies would need to consume only 6.4% of their diet to reach the NOAEC (12.0% to reach the LOAEC), suggesting that the availability of alternative sources of forage may be unlikely to change the risk conclusions.

When considering the available residue data, residues from the thiamethoxam studies (cucumber and pumpkin) exceed the clothianidin CFS NOAEC and LOAEC for up to 19 days at multiple locations and time points. Although none of the normalized mean-measured clothianidin data for pumpkin exceed the colony effects endpoints, the thiamethoxam residues are considered representative of potential residues of clothianidin. The bridging analysis (**Attachment 2**) suggested that some cucurbit crops (*e.g.* cucumber) have higher residues than pumpkin following foliar applications (based on thiamethoxam data). As pumpkin is the only crop available for clothianidin, residues in pumpkin may under predict those for other crops in the crop group.

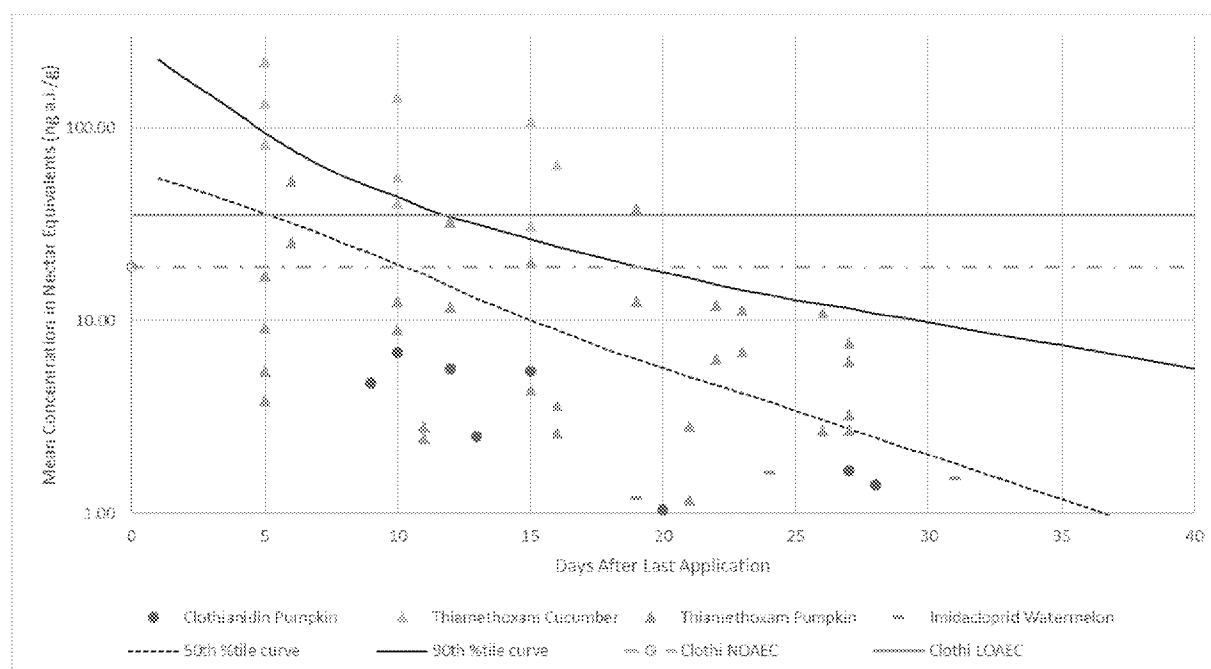


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]. Measured clothianidin (circles), thiamethoxam, (triangles; measured in clothianidin equivalents), dinotefuran (diamonds), and imidacloprid (single dashes) residue data in nectar equivalents (normalized to 0.2 lb c.e./A total application) versus the clothianidin CFS endpoints (19 and 35.5 ng c.e./g for NOAEC and LOAEC, respectively) for the cucurbit crop group. Diagonal curves represent the 50th (dashed) and 90th percentiles (solid) from the Monte Carlo analysis of residue decline kinetics (Attachment 2) using data from all neonicotinoids.

Clothianidin: Soil application

Similar to the foliar residue data, the bridging analysis for residues from soil applications indicated that overall residues for the different tested crops within the cucurbit group and different neonicotinoids can be used to represent residues for clothianidin (and all other neonicotinoids) and all crops within the group. There are several clothianidin studies that examine the residues of nectar and pollen in soil-treated pumpkin (MIRDS 49705901, 49910601, and 49602801) cucumber (MRID 49705901), melon (MRIDs 49705901 and 50154306) and squash (MRID 49705901). Available data for thiamethoxam (MRIDs 49550801 and 50265501), dinotefuran (MRID 49852701) and imidacloprid (MRIDs 49090501 and 50357101) for pumpkin, melon, squash and/or cucumber residue concentration data can be used to also represent exposures from potential clothianidin soil applications to cucurbit crops. Details on these studies and the bridging analysis are provided in **Attachment 2**.

While a Monte Carlo analysis involving residue data and dissipation rate constants was conducted for foliar applications to cucurbits, this approach was not supported for soil applications due to limitations in the dataset (**Attachment 2**). As residue data following soil applications were considered, it became clear that dissipation rate constants often could not be calculated due to the essentially stable residues in pollen and/or nectar. Further, as **Figure 5-6** suggests, a Monte Carlo analysis based on residue declines could not possibly produce curves that would fit the available empirical data. Instead of the

Monte Carlo analysis, the available measured residue data from soil applications for all the neonicotinoid compounds are considered along with the endpoints from the available CFS. Values were normalized to the maximum total (seasonal) clothianidin application rate registered across the cucurbit crop group (*i.e.*, 0.2 lb c.e./A).

Figure 5-6 depicts all the residue data (normalized to total seasonal application rate of 0.2 lb c.e./A) compared to the clothianidin CFS NOAEC and LOAEC endpoints. Mean-measured residues (normalized to total application rate) from soil applications of neonicotinoids to cucurbit crops range from 0.1 to 40.0 ng c.e./g and exceed the NOAEC and LOAEC in 11 (6%) and 4 (2%), respectively, of daily samples. Approximately half the data available are for pumpkins, which generally appear to have lower residues. When that data are excluded from the dataset, the remaining normalized mean-measured residue data exceed the NOAEC and LOAEC in 15% and 6%, respectively of daily samples. Observations of mean (normalized) samples approaching the NOAEC begin shortly after application and continue to exceed the NOAEC up to 57 days following treatment.

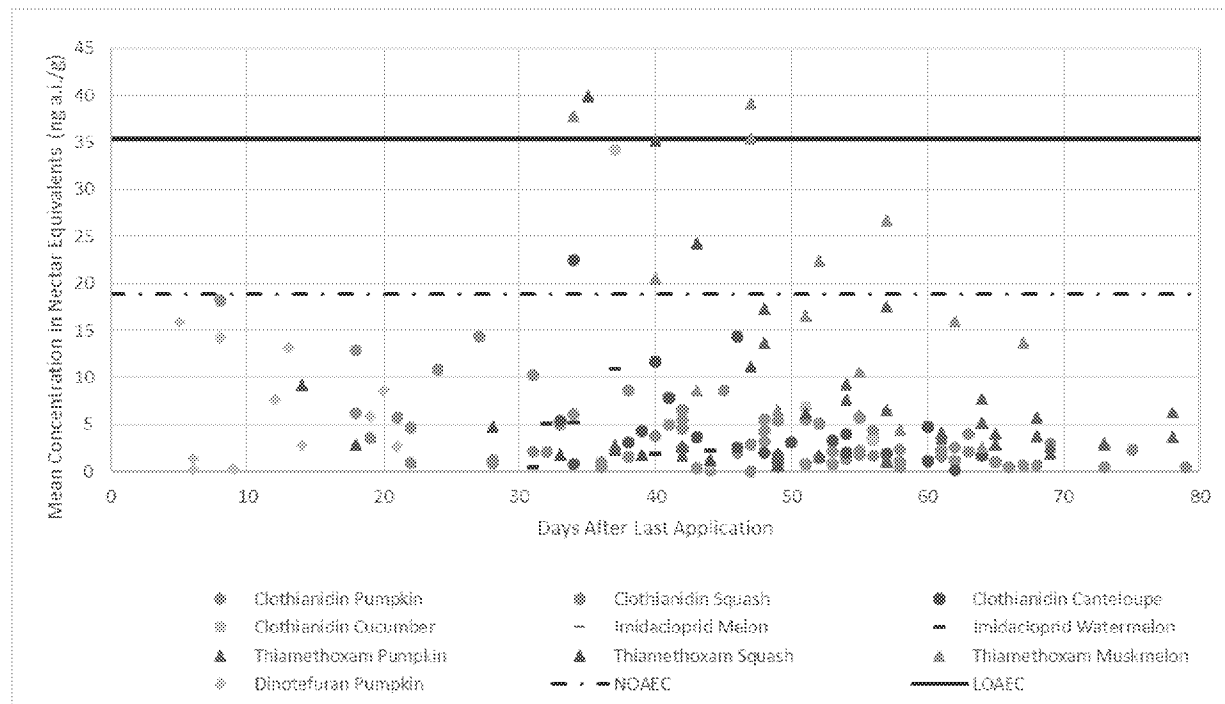


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]. Measured clothianidin (circles), thiamethoxam, (triangles; measured in clothianidin equivalents), dinotefuran (diamonds), and imidacloprid (single dashes) residue data in nectar equivalents (normalized to 0.2 lb c.e./A total application) versus the clothianidin CFS NOAEC and LOAEC endpoints (19 and 35.5 ng c.e./g, respectively) for the cucurbit crop group.

Relatively little of the clothianidin-only data are above the clothianidin CFS NOAEC or LOAEC with only one mean-measured cucumber sample (Fresno, CA) and one mean-measured cantaloupe sample (Mebane, NC) exceeding these endpoints. The cantaloupe data that exceeded the colony-level endpoints were an average of three bee-collected samples (which all had residues below the CFS NOAEC) and one hand-collected sample (that had residues exceeding both the NOAEC and LOAEC). This creates

some uncertainty regarding how the actual range of concentrations in cantaloupe vary and comparisons of hand collected samples (which represent the vast majority of sample data across the different studies), with bee-collected residues. **Figure 5-6** also demonstrates that the majority of clothianidin cucurbit data is for pumpkins, while particularly little data are available for squash and cucumber. The residue bridging strategy (**Attachment 2**) suggests that pumpkin may underestimate cucurbit floral residues compared to other cucurbit crops. In contrast to the clothianidin-only dataset, other neonicotinoid residues (*e.g.* thiamethoxam), exceeded the clothianidin endpoints for multiple crops and locations when normalized to the clothianidin maximum total application rates.

Based on the analysis above, for soil applications, the residues in total nectar equivalents (nectar and adjusted pollen) for registered uses in the cucurbit crop group exceed the clothianidin NOAEC for soil treatment applications at the maximum allowed rates. When considering timing of exposure, clear patterns are not discernable, but residues exceed the NOAEC and LOAEC for more than 57 and 47 days, respectively, following treatment. The analysis above used anther data quantitatively as a direct surrogate for pollen (as suggested by the residue bridging strategy in **Attachment 2**) when pollen data were not collected and only anther data were available. Specifically, anther residues were used for the cucumber data and part of the cantaloupe data for clothianidin (both from MRID 49705901). The residue bridging strategy also suggests further characterizing the anther data qualitatively using a 3x factor as an upper-bound conservative estimate. Using this extrapolation would not change the overall conclusions that the available data suggests potential risks of concerns for bees from soil applications of clothianidin to cucurbit crops.

Using the maximum measured daily mean value (normalized to the total seasonal application rate of 0.2 lb c.e./A) of 40 ng c.e./g, cucurbit floral resources would need to represent >47.6% and >88.9% of the diet of a honey bee colony to exceed the NOAEC and LOAEC, respectively. Based on this analysis, the overall risk conclusion of risk for honey bee colonies feeding on treated cucurbit fields remains but may be diminished where substantial attractive untreated forage exists near the treated field.

Thiamethoxam: **Foliar applications**

The results of the bridging analysis for foliar applications to cucurbits (**Attachment 2**) concludes that overall residues in pollen and nectar for different crops and neonicotinoids can be used to represent all cucurbit crops in the group and all four chemicals, despite some observed intra-crop differences (*e.g.* thiamethoxam residues in pumpkin compared to cucumber). There are two studies that examine residue concentrations in nectar and pollen following foliar-applied thiamethoxam to pumpkins and cucumbers (MRIDs 49804105 and 50265506). Based on the bridging analysis (**Attachment 2**), clothianidin (MRIDs 49602802 and 49910601) and imidacloprid (MRID 50357101) applications to pumpkin and melon can be used to assess exposure to honey bees. For foliar applications, the residue bridging analyses (**Attachment 2**) suggest that crop may have an influence on residue concentrations, whereas the chemical does not have an influence. This is primarily based on the similar concentrations observed across chemical and matrix (*e.g.*, pollen and nectar) for clothianidin and thiamethoxam residues in pumpkin while thiamethoxam residues in nectar and pollen of cucumbers were observed to be consistently higher than thiamethoxam residues in nectar and pollen of pumpkins following foliar applications.

Using the available residue data, distributions for the cucurbit crop group were developed to estimate the 50th, 70th, and 90th percentile residues over time (using a Monte Carlo analysis). The distributions

representing the 50th and 90th percentiles of the data are presented in **Figure 5-7**, along with the measured residue data and colony-level NOAEC and LOAEC endpoints from the available thiamethoxam and clothianidin CFS studies. Residue concentrations were normalized to the maximum total (seasonal) application rate registered across the cucurbit crop group (*i.e.*, 0.15 lb c.e./A). Predicted residues based on the 50th and 90th percentile curve exceeded the thiamethoxam NOAEC of 44 ng c.e./g and the thiamethoxam LOAEC of 81 ng c.e./g. Mean-measured empirical residues (normalized to total application rate) from foliar applications of neonicotinoids to cucurbit crops range from <0.1 to 222 ng c.e./g, with 8 (12%) and 5 (7%) of values above the thiamethoxam NOAEC and LOAEC, respectively (by comparison, 14 (21%) and 10 (15%) of values were above the clothianidin NOAEC and LOAEC, respectively). Observations of mean measured empirical (normalized) values exceeding the thiamethoxam CFS NOAEC and LOAEC persist for up to 16 and 15 days, respectively, while residues exceeded both the clothianidin CFS NOAEC and LOAEC for up to 19 days.

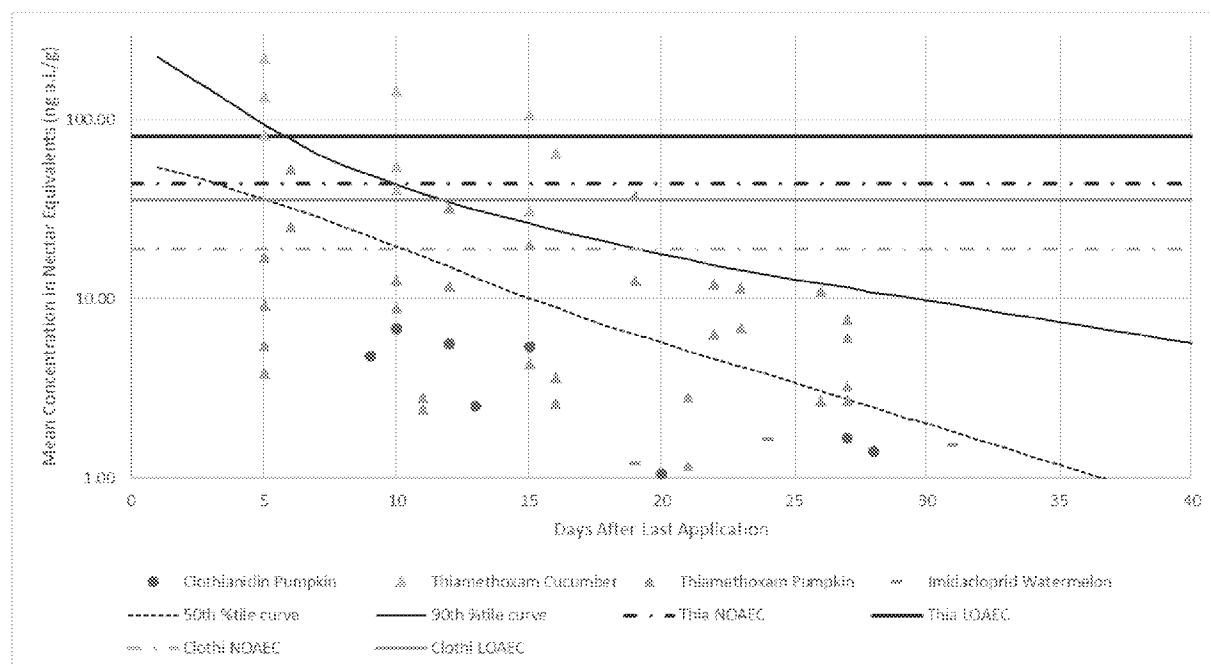


Figure [STYLREF 1 \s]-[SEQ Figure * ARABIC \s 1]. Measured thiamethoxam, (triangles; measured in clothianidin equivalents), clothianidin (circles), dinotefuran (diamonds), and imidacloprid (single dashes) residue data for the cucurbit crop group in nectar equivalents (normalized to 0.15 lb c.e./A total application) versus the thiamethoxam colony-level CFS NOAEC and LOAEC endpoints (44 and 81 ng c.e./g, respectively) and clothianidin NOAEC and LOAEC endpoints (19 and 35.5 ng c.e./g, respectively). Diagonal curves represent the 50th (dashed) and 90th (solid) percentiles from the Monte Carlo analysis of residue decline kinetics (Attachment 2) using data from all neonicotinoids.

Using the distribution curves generated by the Monte Carlo analysis, residues in cucurbit crops remained above the thiamethoxam NOAEC up to 9 days after application and above the clothianidin NOAEC for up to 19 days (90th percentile). Using the 50th percentile data, residues do not exceed the thiamethoxam LOAEC, but do exceed the thiamethoxam NOAEC for 3 days, while the residues for this distribution exceed the clothianidin NOAEC and LOAEC for 10 and 5 days, respectively.

The maximum measured daily mean value (normalized to the total seasonal application rate of 0.15 lb c.e./A) was 222 ng c.e./g. At this concentration in their diet, honey bee colonies would need to consume

>20% of their diet to exceed the thiamethoxam CFS NOAEC, while >37% of the diet would need to be consumed to exceed the thiamethoxam LOAEC. In contrast, at the maximum measured concentrations, bees consuming more than 9% and 16% of their diet would exceed the clothianidin CFS NOAEC and LOAEC endpoints. Based on this analysis, the overall risk conclusion of risk for honey bee colonies feeding on treated cucurbit fields may be unlikely to be affected by the potential dilution of forage from other food sources.

As discussed previously, the total residues of concern of thiamethoxam are composed of both thiamethoxam and clothianidin. In the available thiamethoxam foliar studies with cucurbits, both chemicals occurred in nectar and pollen. In nectar, clothianidin represented 8% of the total residue (on average; range: 2-18%) in cucumber (MRID 49804105) and 14% (on average; range: 14-94%) in pumpkin (MRID 50265506). In pollen, clothianidin represented 12% of the average residue in cucumber and 43% in pumpkin. This indicates that both the thiamethoxam and clothianidin CFS endpoints should be considered in evaluating the risk of cucurbits. Since residues exceed both the clothianidin and thiamethoxam CFS NOAEC and LOAEC values, the conclusion that this use poses a risk to honey bee colonies is not influenced greatly by the proportion of thiamethoxam and clothianidin in the total residues.

As discussed previously in the effects characterization, one Tier II (*i.e.*, tunnel) study is available for thiamethoxam applications to melons located in Italy (MRID 49158904; supplemental classification). In this study, thiamethoxam was applied via spray at a rate of 0.089 lb a.i./A, which is similar to the maximum single application rate allowed for cucurbits (*i.e.*, 0.075 lb a.i./A), but does not cover the maximum total rate allowed on the label (0.15 lb a.i./A from two applications of 0.075 lb a.i./A). Two different treatments were established, one where applications were made 5 days before bloom and for the other, applications were 10 days before bloom. Each treatment (and the control) contained 3 replicates. In both treatments, increased adult bee mortality was observed, as well as a decrease in flight intensity. A decrease in brood was observed in the controls and treatments, suggesting stress due to the tunnels. Therefore, impacts on colony condition/strength are not considered here. The observations of increased mortality are consistent with Tier I effects data suggesting that exposures to thiamethoxam may result in mortality to adult bees.

Thiamethoxam: Soil Application

Similar to the foliar residue data, the bridging analysis for residues from soil applications indicated that overall residues for different crops within the cucurbit group and different neonicotinoids can be used to represent residues for thiamethoxam (and all other neonicotinoids) and across all crops within the group, despite some observed intra-crop differences (*e.g.* thiamethoxam residues in pumpkin compared to cucumber). There are several thiamethoxam studies that examine the residues of nectar and pollen in soil-treated pumpkin, cucumber, melon and squash (MRIDs 49550801 and 50265501). Available data for clothianidin (MRIDs 49705901, 49910601, 49602801, 49705901, 49705901, 50154306, 49705901), dinotefuran (MRIDs 49852701) and imidacloprid (MRIDs 49090501 and 50357101) pumpkin, melon, squash and/or cucumber residue concentration data can be used to also represent exposures from thiamethoxam soil applications to cucurbit crops. Details on these studies and the bridging analysis are provided in **Attachment 2**.

While a Monte Carlo analysis involving residue data and dissipation rate constants was conducted for foliar applications to cucurbits, this approach was not supported for soil applications due to limitations

in the dataset (**Attachment 2**). As residue data following soil applications were considered, it became clear that dissipation rate constants often could not be calculated due to the essentially stable residues in pollen and/or nectar. Further, as **Figure 5-8** demonstrates, a Monte Carlo analysis based on residue declines could not possibly produce curves that would fit the available empirical data. Instead of the Monte Carlo analysis, the available measured residue data from soil applications for all the neonicotinoid compounds are considered along with the colony-level NOAEC and LOAEC from the available CFS. Values were normalized to the thiamethoxam maximum total (seasonal) application rate registered across the cucurbit crop group (*i.e.*, 0.15 lb c.e./A).

Because thiamethoxam transforms to clothianidin within plants, the total residue is represented as both thiamethoxam and clothianidin. In the available thiamethoxam soil treatment residue studies for cucurbits, both chemicals occurred in nectar and pollen. In nectar, clothianidin represented an average of 22% of the residues in muskmelon, 29% in pumpkin and 18% in squash (MRID 50265501). In pollen, clothianidin represented 48% of the residue (on average) in muskmelon and pumpkin and 33% of the residue in squash. In another study with cucumber, residues in nectar ranged 11-33% and 14-20% in pollen (MRID 49550801). This indicates that both the thiamethoxam and clothianidin CFS endpoints should be considered in evaluating the risk of cucurbits.

Figure 5-8 below depicts all the residue data (normalized to total seasonal application rate of 0.15 lb c.e./A) compared to the thiamethoxam and clothianidin colony-level CFS NOAEC and LOAEC endpoints. Overall, no mean measured residues exceed the thiamethoxam NOAEC or LOAEC or the clothianidin LOAEC. Seven daily mean measurements (4%) exceed the clothianidin NOAEC, however. Approximately half the data available are for pumpkins, which generally appear to have lower residues. When these data are excluded from the dataset, the remaining normalized mean-measured residue data exceed the clothianidin NOAEC in 10% of daily mean samples.

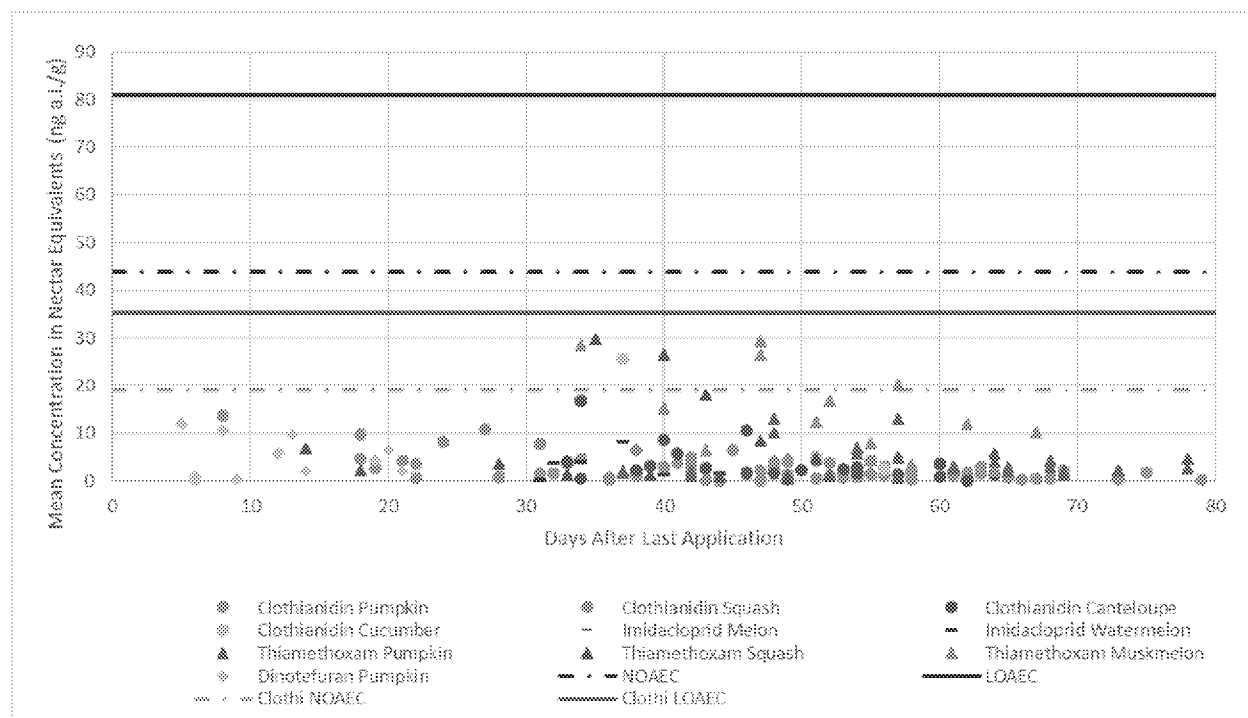


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]. Measured thiamethoxam, (triangles; measured in clothianidin equivalents), clothianidin (circles), dinotefuran (diamonds), and imidacloprid (single dashes) residue data in nectar equivalents (normalized to 0.15 lb c.e./A total application) versus the thiamethoxam and clothianidin colony-level CFS NOAEC and LOAEC endpoints for the cucurbit crop group.

Based on the analysis above, residues in total nectar equivalents (nectar and adjusted pollen) for registered uses in the cucurbit crop group exceed the clothianidin NOAEC for soil applications at the maximum allowed rates, but do not exceed the clothianidin LOAEC or either of the thiamethoxam endpoints. When considering timing of exposure, clear patterns are not discernable, but measured residues exceed the clothianidin NOAEC for up to 47 days following treatment.

The preceding analysis used anther data quantitatively as a direct surrogate for pollen (as suggested by the residue bridging strategy in **Attachment 2**) when pollen data were not collected and only anther data are available. Specifically, anther residues were used for the cucumber data and part of the cantaloupe data for clothianidin (both from MRID 49705901). The residue bridging strategy also suggests further characterizing the anther data qualitatively using a 3x factor as an upper-bound conservative estimate. Using this extrapolation would not change the overall conclusions that measured residues exceed the colony-level NOAEC based on a total seasonal application rate of 0.15 lb c.e./A. Overall, the available information suggests potential for risks of concerns for bees from soil applications of thiamethoxam to cucurbit crops based on exceedances of the clothianidin CFS NOAEC endpoints.

The maximum measured daily mean value (normalized to the total seasonal application rate of 0.15 lb c.e./A) was 30 ng c.e./g. At this concentration, more than 100% of a honey bee colony's diet would need to come from treated cucurbit floral resources to reach the thiamethoxam CFS NOAEC, while >68% of the diet would need to come from these sources to reach the clothianidin CFS NOAEC. Based on this analysis, the overall risk conclusion of risk for honey bee colonies feeding on treated cucurbit fields may be affected where attractive untreated forage exists near the treated field.

A supplemental field study (MRID XXXX) that was conducted in Spain is available where bees were exposed to thiamethoxam from soil applications to melons (at 0.18 lb a.i./A, which is comparable to the max rate of 0.15 lb a.i./A). In this study, applications were made either 1 or 33 days before flowering. An increase in mortality was observed in applications made 1 day before flowering; while no significant effect was observed for the application made 33 d before exposure. This study is limited by its design, which did not include true replication. Variability was accounted for by placing 4 colonies on a single field that was treated.

In 2018, a bee kill incident (I031569) was reported after an application of thiamethoxam to watermelons in CA. Residues of thiamethoxam were detected on dead bees. The legality and certainty of this incident is undetermined. This incident was associated with an application of the formulated product, Platinum (registration number 100-1291), which is only registered for soil applications of thiamethoxam.

5.2.2.3 Orchard Tree Crops

Orchard crops cover several crop groups, including pome fruit (pears and apples), stone fruit (*e.g.*, peaches, plums, cherries), tree nuts (*e.g.*, almonds, pecans), citrus (*e.g.*, oranges, lemons) and tropical

fruit (e.g., pomegranate). According to USDA (2017) many orchard crops require bee pollination and use managed pollinators, including pome fruit, stone fruit and tree nuts. Citrus and some tropical fruits do not require or use managed bees; however, they are attractive to honey bees. This analysis considers exposures of honey bees to thiamethoxam and clothianidin through pollen and nectar of treated tree crops.

Clothianidin is registered for use on all orchard crop group constituents. It may be applied via foliar or soil applications. Pre-bloom applications are not allowed on any crop. **Table 5-20** summarizes the foliar and soil application information for clothianidin for each crop group. Thiamethoxam is registered for foliar applications on all orchard crop groups. For soil applications, thiamethoxam is only registered on citrus. Thiamethoxam has no pre-bloom restrictions. **Table 5-21** summarizes the foliar and soil applications for each crop group for thiamethoxam.

Table [STYLEREf 1 \s]-20. Foliar and soil application rates (in lb c.e./A) and number of applications (x n) for clothianidin on orchard crops (based on current labels).

Orchard crop group	Foliar, pre-bloom	Foliar, post-bloom	Soil, pre-bloom	Soil, post-bloom
Pome fruit	NR	0.2 x 1	NR	0.2 x 1
Stone fruit	NR	0.2 x 1	NR	0.2 x 1
Citrus	NR	0.2 x 1	NR	0.2 x 2 (4 mo interval)
Tree nuts	NR	0.1 x 2	NR	0.1 x 2
Tropical fruits	NR	0.1 x 2	NR	0.1 x 2

NR = not registered

Table [STYLEREf 1 \s]-21. Application rates (in lb c.e./A)* and number of applications (x n) for thiamethoxam on orchard crops (based on current labels). Thiamethoxam rate expressed as clothianidin equivalent.

Orchard crop group	Foliar	Soil
Pome fruit	0.074 X 3	NR
Stone fruit	0.074 x 2	NR
Citrus	0.075 x 2	0.15 x 1
Tree nuts	0.053 x 2	NR
Tropical fruits	0.053 x 3	NR

*Clothianidin-equivalent rates

This section describes the lines of evidence associated with the assessment of risks of clothianidin and thiamethoxam to honey bee colonies from foliar applications to orchard crops.

For clothianidin, post-bloom foliar applications to orchard crops represent a low risk to honey bee colonies. This is based on the observation that measured residues from 6 different crops taken from 24 different locations are all below the clothianidin CFS NOAEC. **For post-bloom soil applications to orchard crops, there is moderate evidence of risk to honey bee colonies foraging on treated fields.** Residue data from orange and lemon trees treated via soil (179 and 156 d after application, respectively) are above the NOAEC and LOAEC (by 2.6x and 1.4x, respectively). The existing data set is limited to only 12 samples for post-bloom applications, so there is some uncertainty as to the magnitude and duration of time where residues are expected to exceed colony level endpoints. The lines of evidence for the clothianidin risk conclusions are summarized in **Table 5-22** and discussed below.

For thiamethoxam, pre-bloom foliar applications represent a risk to honey bee colonies, with strong weight of evidence to support this risk conclusion. Residues from multiple studies and locations (for oranges and apples) are well above the CFS NOAEC and LOAEC endpoints, dissipating below these levels after multiple weeks. There are also multiple field studies that involve observations of bee mortality following foliar applications to pear, apple and peach orchards. Finally, there are 13 incidents involving bee kills, which are assumed to have followed foliar applications of thiamethoxam. **As with clothianidin, post-bloom foliar applications of thiamethoxam represent a low risk to honey bee colonies,** with all residues from 6 crops and 24 locations being below CFS NOAECs. For soil applications to citrus (only registered use), residues that could be considered pre-bloom and post-bloom exceed colony level endpoints. Residues from multiple crops (lemon and orange) and 5 sites exceed the clothianidin CFS NOAEC, while only residues from 2 sites exceed the thiamethoxam NOAEC. **For pre-bloom soil applications, there is strong evidence of risk.** As discussed for clothianidin, there is a limited number of samples representing post-bloom applications (2 of which exceed the clothianidin NOAEC). In addition, none of the residues exceed the thiamethoxam NOAEC or the clothianidin or thiamethoxam LOAECs. **Therefore, for post-bloom, soil applications of thiamethoxam to citrus, the evidence of risk is weakest.** The lines of evidence for the thiamethoxam risk conclusions are summarized in **Table 5-23** below.

Table [STYLEREf 1 \s]-22. Lines of evidence considered in risk call for applications of clothianidin to orchards.

Line of evidence		Foliar applications, post-bloom (LOW Risk)		Soil applications, post-bloom (Moderate evidence of risk)	
Clothianidin specific residue data		apple, almond, peach		Orange, lemon	
Residue data for other chemicals		Imidacloprid: cherry Dinotefuran: peach, cherry Thiamethoxam: Cherry, peach, plum		Thiamethoxam: Orange, lemon	
Measured data	Exceedance Attribute	NOAEC	LOAEC	NOAEC	LOAEC
	Frequency: Number daily mean residue values > NOAEC & LOAEC	None	None	4	2
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	None	None	179	156
	Magnitude: Ratio of Max to NOAEC & LOAEC (% of diet required to reach NOAEC & LOAEC)	0.72X (not calculated)	0.39X (not calculated)	2.6X (38%)	1.4X (71%)
Crop Attractiveness* & Bloom Duration		Attractive or highly attractive. Bloom duration varies depending on crop/variety.			
Managed pollinators*		Managed pollinators required for pome fruit, stone fruit, tree nuts and tropical fruit, but not for citrus. Honey production for some commercial beekeepers (including citrus)			
Ecological incidents		None reported			
Spatial extent of risk (annual acres treated)		Tree nuts: <25,625 (ave and max) Pome fruit: 2,720-10,915 (ave); 24,550 (max) Stone fruit: 5,644-6,472 (ave), 11,288-13,358 (max) Oranges: <6,130 (ave), <15,320 (max) Figs: 860 (ave), 1,290 (max)			
Other considerations		Residue data represent 6 different crops, and 24 different locations. All residues are below the colony level NOAEC.		Residue data are only available for citrus crops. It is assumed that residues in oranges and lemons are representative of all other orchard crop groups.	

*Based on USDA 2017

Table [STYLEREf 1 \s]-23. Lines of evidence considered in risk call for applications of thiamethoxam to orchards.

Line of evidence		Foliar applications, pre-bloom (Strong Evidence of Risk)**				Foliar applications, post-bloom (LOW Risk)				Soil applications, pre- and post-bloom (citrus only) (strong evidence of risk for pre-bloom; weak evidence of risk for post-bloom)			
Thiamethoxam specific residue data		Apples, oranges Data are not available for tree nuts, stone fruit or tropical fruits				Cherry, peach, plum				Orange, lemon			
Residue data for other chemicals		Imidacloprid oranges				Clothianidin: apple, almond, peach, Imidacloprid: cherry, Dinotefuran: peach, cherry				Clothianidin: Orange, lemon			
Percent of clothianidin present in total residues (average)		Nectar: 37% Pollen: 40%				1-94%				30%			
Measured data	Exceedance Attribute	Clothi NOAEC	Clothi LOAEC	Thia NOAEC	Thia LOAEC	Clothi NOAEC	Clothi LOAEC	Thia NOAEC	Thia LOAEC	Clothi NOAEC	Clothi LOAEC	Thia NOAEC	Thia LOAEC
	Frequency: Number daily mean residue values > NOAEC & LOAEC	20(0.11) 23 (0.22)	14(0.11) 21(0.22)	11(0.11) 20(0.22)	8(0.11) 11(0.22)	None	None	None	None	16	8	5	1
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	21 (0.11) 34 (0.22)	21(0.11) 21(0.22)	21(0.11) 21(0.22)	13(0.11) 21(0.22)	None	None	None	None	156	156	60	16
	Magnitude: Ratio of Max to NOAEC & LOAEC* (% of diet required to reach NOAEC & LOAEC)	0.11: 44x (2.3%) 0.22: 88x (1.1%)	0.11: 24x (4.2%) 0.22: 47x (2.1%)	0.11: 19x (5.2%) 0.22: 38x (2.6%)	0.11: 10x (9.6%) 0.22: 21x (4.8%)	0.22: 0.79x (NC)	0.22: 0.42x (NC)	0.22: 0.34x (NC)	0.22: 0.18x (NC)	6.7x (15%)	3.6x (28%)	2.9x (35%)	1.6x (64%)
	Duration: Max Interval (d) since	26 (0.11) 35 (0.22)	20 (0.11)	18 (0.11)	12 (0.11)	Not applicable				Not applicable			

Line of evidence		Foliar applications, pre-bloom (Strong Evidence of Risk)**				Foliar applications, post-bloom (LOW Risk)	Soil applications, pre- and post-bloom (citrus only) (strong evidence of risk for pre-bloom; weak evidence of risk for post-bloom)
Modeled Data (50 th percentile)	application with NOAEC/LOAEC exceedance		27 (0.22)	25 (0.22)	18 (0.22)		
	Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC	0.11: 18x (5.7%) <hr/> 0.22: 35x (2.8%)	0.11: 9.5x (11%) <hr/> 0.22: 19x (5.3%)	0.11: 7.6x (13%) <hr/> 0.22: 15x (6.5%)	0.11: 4.1x (24%) <hr/> 0.22: 8.3x (12%)		
Crop Attractiveness* & Bloom Duration		Attractive or highly attractive for all crops. Bloom duration varies depending on crop/variety.					
Managed Pollinators*		Managed pollinators required for pome fruit, stone fruit, tree nuts and tropical fruit, but not for citrus. Honey production for some commercial beekeepers (including citrus)					Managed pollinators not required; however, honey production may be relevant to citrus.
Tier III Data		In a field study involving applications of thiamethoxam to pears (48584701), increased adult mortality was observed in applications made 1, 3 and 5 days before bloom, but not 8 or 11 days before bloom. Thiamethoxam was applied at a rate of 0.085 lb a.i./A, which is above the maximum allowed single application rate for pome fruit (0.074 lb a.i./A).					None
Ecological incidents		13 bee kill incidents (with certainty of either possible or probable) have been reported in association with thiamethoxam applications to orchards (cherries, pears, lemons and unspecified crop).					It is unlikely that the reported incidents involved soil applications.
Spatial extent of risk (annual acres treated)		Tree nuts: <1,780 (ave), <4,450 (max) Pome fruit: 27,270 (ave), 84,600 (max) Stone fruit: 18,000-20,000 (ave), 48,800-49,800 (max) Citrus: 116,000 (ave), 212,000 (max) Tropical fruit: no usage data available					Citrus: 116,000 (ave); 212,000 (max)

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*Maximum measured value represents 1 day after application.

**Based on USDA 2017

***Maximum total rates for thiamethoxam applications to orchards range 0.11-0.22 lb c.e./A. Table presents information for 0.11 lb c.e./A, as indicated by (0.11) and 0.22 lb c.e./A, as indicated by (0.22).

NC = not calculated

Another consideration with respect to potential risk is the spatial extent of risk. Annual usage data available for clothianidin and thiamethoxam applied to orchard crops (via foliar or soil) are summarized in **Table 5-24**. These data indicate that tens of thousands of lbs of clothianidin are and hundreds of thousands of lbs of thiamethoxam are applied per year to orchards in the US. Of all orchard crops, the greatest amount of clothianidin applied is to almonds, apples, peaches, pears, and pecans (1,000 lbs applied each per year). Based on the available usage data, tree nuts and pome fruit represent the crop groups with the largest amount of clothianidin applied per year. For thiamethoxam, the greatest amount applied per year is to oranges (10,000 lbs/year), followed by apples (2,000 lbs/year) and grapefruit (2,000 lbs/year). Based on the available usage data, citrus and pome fruit represent the crop groups with the largest amount of thiamethoxam applied per year and the largest percent of crop treated acres (PCT) per year. When the total number of acres of bearing orchards is considered (**Table 5-25**), this translates to an annual average of approximately 50,000 acres of orchards treated with clothianidin, with a maximum of 80,000 lbs/year, with the majority of the treated acres represented by pome fruit. For thiamethoxam, an annual average of approximately 165,000 acres of orchards are treated, with a maximum of 350,000, where the majority of the treated acres are represented by citrus. As discussed above, there is a difference in risk based on application method and timing; *i.e.*, post-bloom foliar applications are a low risk while soil applications and pre-bloom foliar applications represent a risk. The extent to which acres treated represent post-bloom foliar applications vs. soil or pre-bloom foliar applications (for thiamethoxam only) is unknown. In other words, the spatial footprint of potential risks to bees expressed in **Table-25** is likely smaller because of post-bloom foliar applications.

Table [STYLEREf 1 \s]-24. Estimated annual usage and percent crop treated (PCT) of clothianidin and thiamethoxam applied via foliar or soil applications (source: SLUAs) – Reporting Time 2005-2014.

Crop	Clothianidin			Thiamethoxam		
	Lbs a.i. applied per year	PCT (annual average)	PCT (annual max)	Lbs a.i. applied per year	PCT (annual average)	PCT (annual max)
Almonds	1,000	<2.5	<2.5	NA	NA	NA
Apples	1,000	<2.5	5	2,000	5	20
Cherries	NA	NA	NA	1,000	10	25
Figs	<500	10	15	NA	NA	NA
Grapefruit	NA	NA	NA	2,000	25	65
Lemons	NA	NA	NA	<500	5	10
Oranges	<500	<1	<2.5	10,000	15	25
Peaches	1,000	5	10	1,000	5	15
Pears	1,000	5	15	1,000	20	35
Pecans	1,000	<2.5	5	<500	<2.5	5
Pistachios	NA	NA	NA	<500	<1	<2.5
Plums/Prunes	<500	<1	<2.5	<500	<2.5	<2.5
Pomegranates	<500	<2.5	<2.5	NA	NA	NA
Tangerines	NA	NA	NA	<500	5	10
Walnuts	<500	<2.5	<2.5	NA	NA	NA

NA = not available

Table [STYLEREf 1 \s]-25. Estimated annual acres treated of clothianidin applied via foliar or soil applications.

Group	Crop	Bearing Acres*	Clothianidin		Thiamethoxam	
			Annual Average acres treated	Annual Max acres treated	Annual Average acres treated	Annual Max acres treated
Tree nuts	Almonds	780,000	<19,500	<19,500	NA	NA
	Pecans	NA	NA	NA	NA	NA
	Pistachios	178,000	NA	NA	<1,780	<4,450
	Walnuts	245,000	<6,125	<6,125	NA	NA
	Total:		<25,625	<25,625	<1,780	<4,450
Pome fruit	Apples	327,800	<8,195	16,390	16,390	65,560
	Pears	54,400	2,720	8,160	10,880	19,040
	Total:		2,720-10,915	24,550	27,270	84,600
Stone fruit	Cherries	123,300	NA	NA	12,330	30,825
	Peaches	112,880	5,644	11,288	5,644	16,932
	Plums/Prunes	82,780	<828	<2,070	<2,070	<2,070
	Total:		5,644-6,472	11,288-13,358	17,974-20,044	47,757-49,827
Citrus	Grapefruit	73,300	NA	NA	18,325	47,645
	Lemons	55,000	NA	NA	2,750	5,500
	Oranges	613,000	<6,130	<15,320	91,950	153,250
	Tangerines	52,100	NA	NA	2,605	5,210
	Total:		<6,130	<15,320	115,630	211,605
Tropical fruit	Figs	8,600	860	1,290	NA	NA
	Pomegranates	NA	NA	NA	NA	NA

*From USDA 2017

**From SLUA

NA = not available

Clothianidin: Foliar Applications (post-bloom)

Based on the bridging analysis (**Attachment 2**), the available orchard residue concentration data can be bridged across crop and chemical. Clothianidin residue studies are available for post-bloom applications to almonds (MRID 50154302), apples (MRID 50154304) and peaches (MRID 50154303). Data available for thiamethoxam (MRID 50096606), dinotefuran (MRIDs 50145706 and 50456901) and imidacloprid (MRID 49535601) are also used to further characterize exposure of post-bloom foliar applications to honey bee colonies.

Figure 5-9 depicts total residues from post-bloom soil applications made at 0.2 lb c.e./A. In these studies, applications were made between 140-324 d before bloom. All residues are well below the clothianidin NOAEC. This indicates that post-bloom applications of clothianidin to orchard crops pose a

low risk to honey bee colonies. Since residues represent a variety of crops and locations, there is limited uncertainty associated with the low risk conclusion.

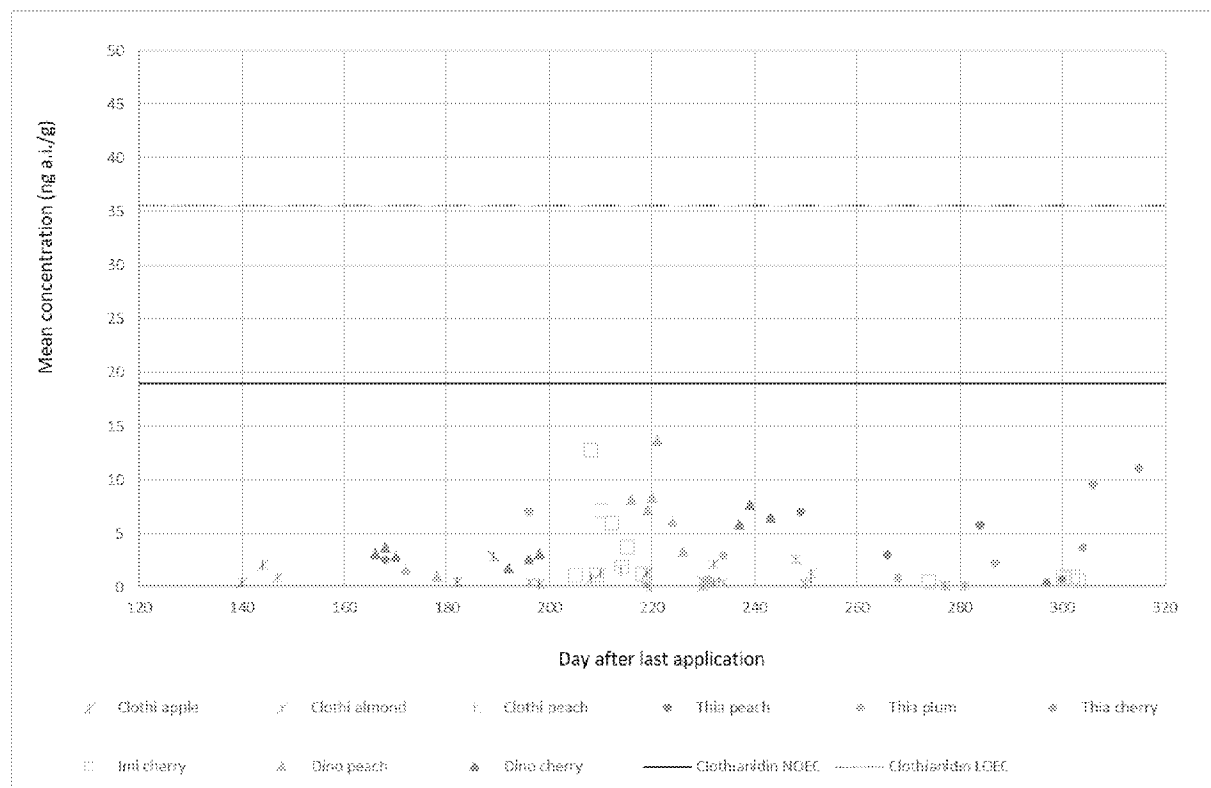


Figure [STYLERE 1 \s]-[SEQ Figure * ARABIC \s 1]. Measured neonicotinoid residue data in orchard crops (normalized to 0.2 lb c.e./A) from post-bloom, foliar applications. Also depicted are the clothianidin colony level NOAEC and LOAEC. Residues represents nectar equivalents (sum of nectar and adjusted pollen residues).

Clothianidin: Soil Applications (post-bloom)

Based on the bridging analysis (**Attachment 2**), the available orchard data are bridged across crop. Residue data are available for oranges and lemons treated with clothianidin (including both pre- and post-bloom applications; MRIDs 49317901 and 50478201). Since data are also bridged across chemicals, the available thiamethoxam (MRIDs 49881001, 49881002, and 49950101) residue data are also used to characterize risks of clothianidin to honey bees.

Residue concentrations are normalized to the total application rate over the course of a given season. Therefore, they are representative of the maximum clothianidin rates for stone fruit and pome fruit (*i.e.*, 0.2 lb c.e./A x 1 application per season) and tree nuts and tropical fruits (*i.e.*, 0.1 lb c.e./A x 2 applications per season). For citrus, there are Section 18 emergency exemption registrations in Florida and Texas which include restrictions to applications past October 31 through bloom (blooming time variable by crop and location) at a maximum rate of 0.2 lb c.e./A. Two applications are allowed at that rate, but with a four-month interval. For all other orchard crops, clothianidin is registered for post-bloom soil applications at a maximum seasonal total rate of 0.2 lb c.e./A.

Figure 5-10 depicts the total residue concentrations, adjusted to the maximum soil application rate allowed for clothianidin (*i.e.*, 0.2 lb c.e./A). There is some uncertainty for citrus in FL and TX, which allows applications of 0.2 lb a.i./A at 4 months apart, so residues may be higher for these locations. This figure depicts pre- and post-bloom residue data. There is no defined time period that represents “post-bloom” applications. In other orchard residue studies (involving foliar applications), post-bloom applications occurred ≥ 140 d before bloom. Residues measured after 140 d exceeded the clothianidin CFS NOAEC and LOAEC (*i.e.*, up to 179 and 156 d, respectively). Therefore, post-bloom, soil applications of clothianidin to orchard crops represent a risk to honey bee colonies.

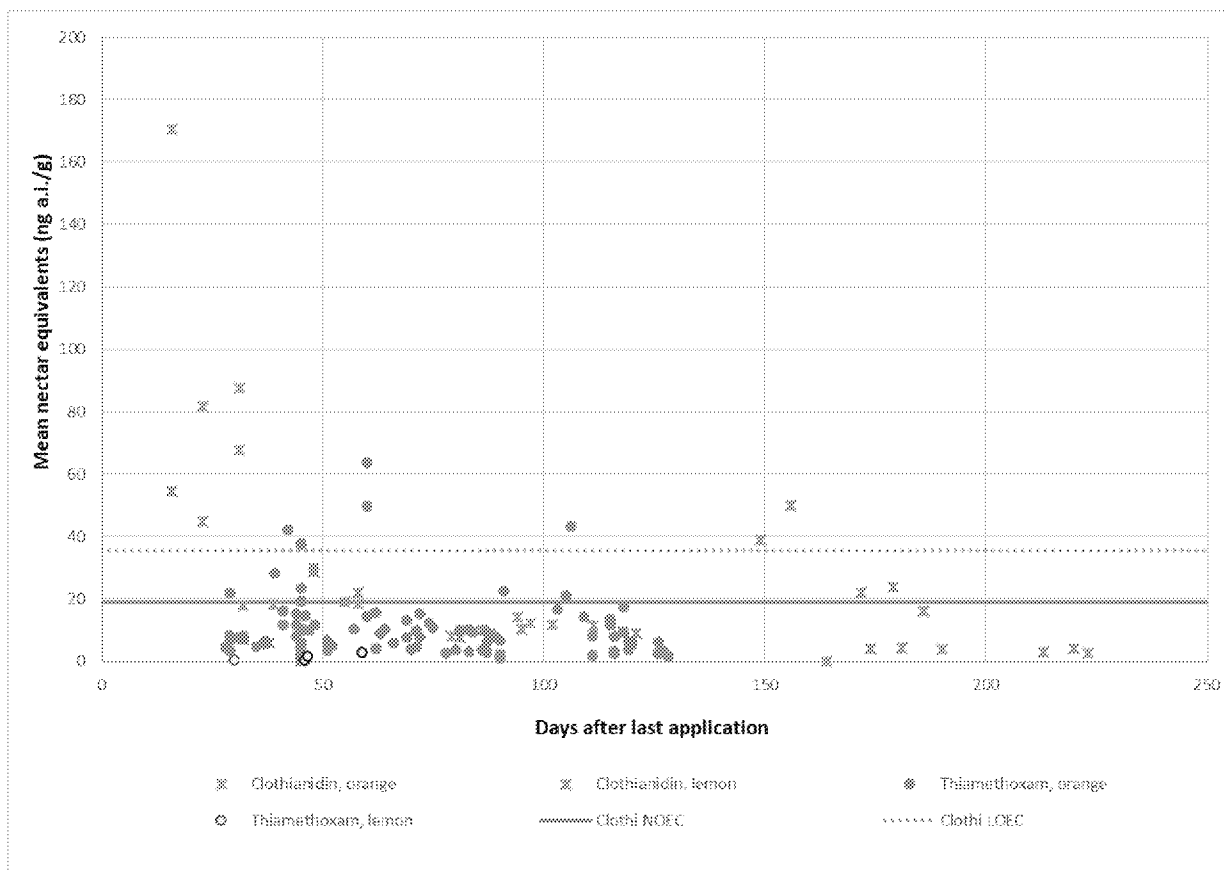


Figure [STYLeref 1 \s]-[SEQ Figure * ARABIC \s 1]. Measured neonicotinoid residue data in citrus (normalized to 0.2 lb c.e./A) from soil applications. Also depicted are clothianidin colony-level NOAEC and LOAEC. Residues represents nectar equivalents (sum of nectar and adjusted pollen residues). Note that the post-bloom application window is assumed to occur at approximately 140-364 d before bloom.

When considering the potential risk, some assumptions of the approach should be considered:

- It is assumed that the nectar and pollen from treated crops are the only sources of clothianidin exposure and that there is no dilution of exposure concentrations from food sources with lower concentrations. This dilution could come in the form of foraging on nectar and pollen from other orchards that are not treated or on other plants that are not treated.
 - o Given the magnitude of residues, $\geq 38\%$ of total food from treated orchards would be required to exceed the colony level NOAEC, suggesting that dilution of concentrations from other sources may not have an influence on the risk conclusion.
- It is assumed that available residue data for lemons and oranges are representative of residues in other orchard crop groups. Since residue data for foliar pre- and post-bloom applications do not indicate a discernable difference between orchard crops from different groups, this assumption does not seem to influence risk conclusions.
- The time period representing when post-bloom applications occur is not clearly defined. As discussed above, this window is assumed to occur between 140 – 364 d before bloom. A limited number of samples (12) are available for this time window from studies involving soil applications to orchard crops (Figure 5-10). Residues exceed the NOAEC and LOAEC; however, the limited number of samples from this time period leads to uncertainty as to how long

residues may be expected to exceed these endpoints and the upper bound of residues relative to the endpoints. In summary, there are still risk concerns, but the characterization related to the magnitude of residues and duration of exceedance is not well understood due to limited number of samples.

Thiamethoxam: Foliar Applications

Based on the bridging analysis (**Attachment 2**), the available orchard data are bridged across crop and chemical. Because of the influence of application timing, data for pre-bloom and post-bloom applications are kept separate. As discussed above, thiamethoxam is registered for pre- and post-bloom foliar applications to all crops at maximum rates (total) ranging 0.11-0.22 lb c.e./A (clothianidin-equivalents). Pre-bloom residue data are available for thiamethoxam applications to apples and oranges as well as post-bloom residue data for stone fruit. As discussed in **Attachment 2** the available foliar application data do not suggest a difference in residues between different orchard crops. Therefore, other data available for clothianidin, dinotefuran and imidacloprid are also used to characterize risk of foliar applications to honey bee colonies.

Figures 5-11 and 5-12 depict the total residues (based on residues from nectar and pollen, with pollen adjusted to nectar equivalents by dividing by 20; details provided in **Attachment 1**), normalized to the maximum pre-bloom foliar application rates allowed for thiamethoxam on orchard crops (*i.e.*, 0.22 and 0.11 lb c.e./A, respectively). These figures also depict the clothianidin and thiamethoxam CFS colony-level NOAEC and LOAEC (clothianidin: 19 and 35.5 ng c.e./g, respectively; thiamethoxam: 44 and 81, respectively). **Table 5-23** summarizes the number of days over which residue concentrations exceed the clothianidin and thiamethoxam NOAECs and LOAEC values at each of the maximum application rates. When considering these residue data, the maximum residues were 1680 and 840 ng c.e./g for the 0.22 and 0.11 lb c.e./A rates, respectively. These residues are 1-2 orders of magnitude greater than the thiamethoxam and clothianidin CFS colony-level toxicity endpoints. To dilute residues below the clothianidin NOAEC, bees would need to forage <1% of their total food from orchards treated with 0.22 lb c.e./A and <2% of total food at the 0.11 lb c.e./A rate. **Figures 5-11 and 5-12** also depict the median residue decline curves that are estimated based on residues in nectar and pollen (adjusted to nectar equivalents). Based on this decline curves, residues exceed the CFS endpoints for 1-5 weeks (depending upon the rate and endpoint).

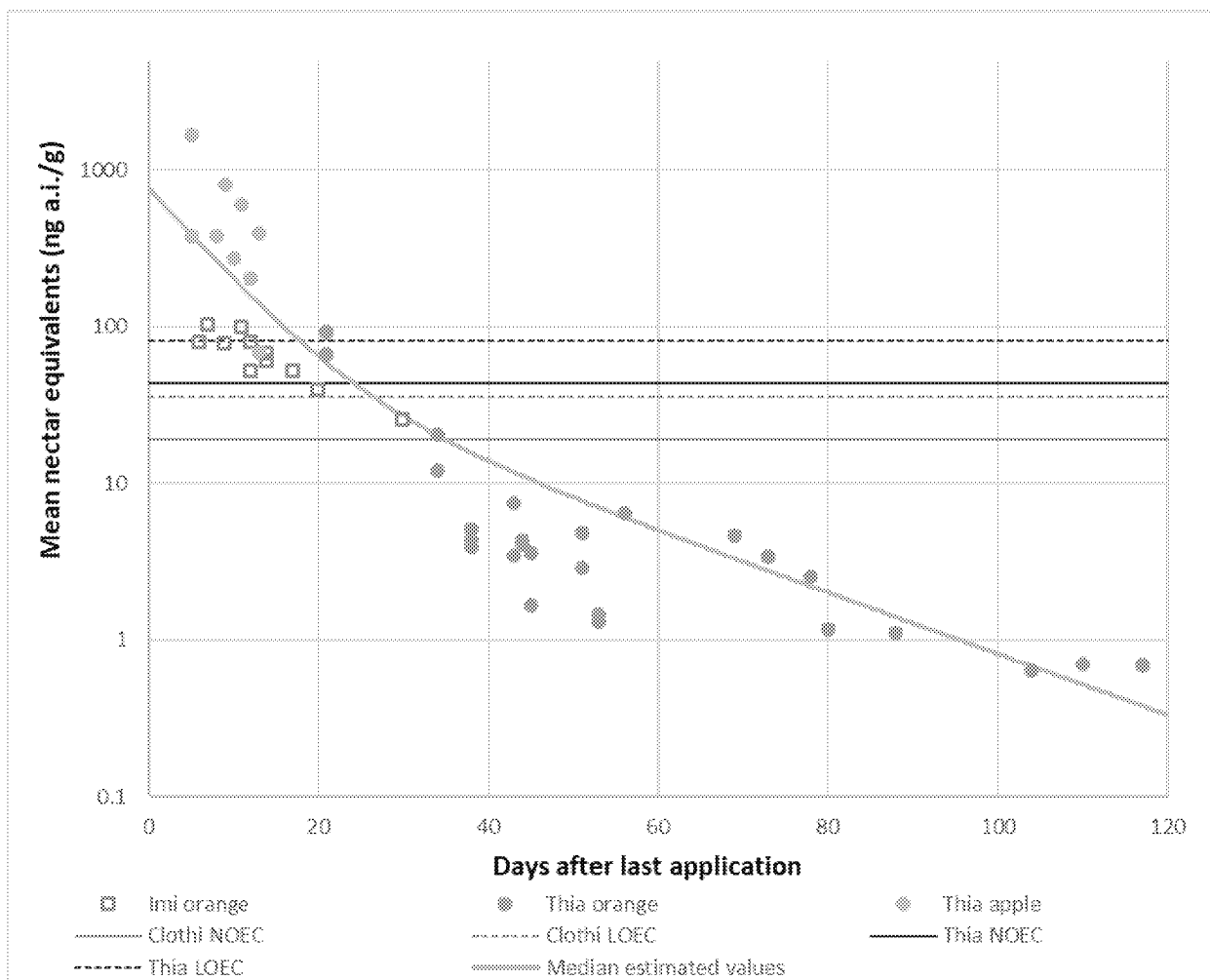


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]1. Measured neonicotinoid residue data in orchard crops (normalized to 0.22 lb c.e./A as clothianidin equivalents; highest total application rate for orchard crops) from pre-bloom, foliar applications. Also depicted are the clothianidin and thiamethoxam colony-level NOAECs and LOAECs. Residues represents nectar equivalents (sum of nectar and adjusted pollen residues). The residue decline curve depicted on this figure (green line) represents the median estimated residues.

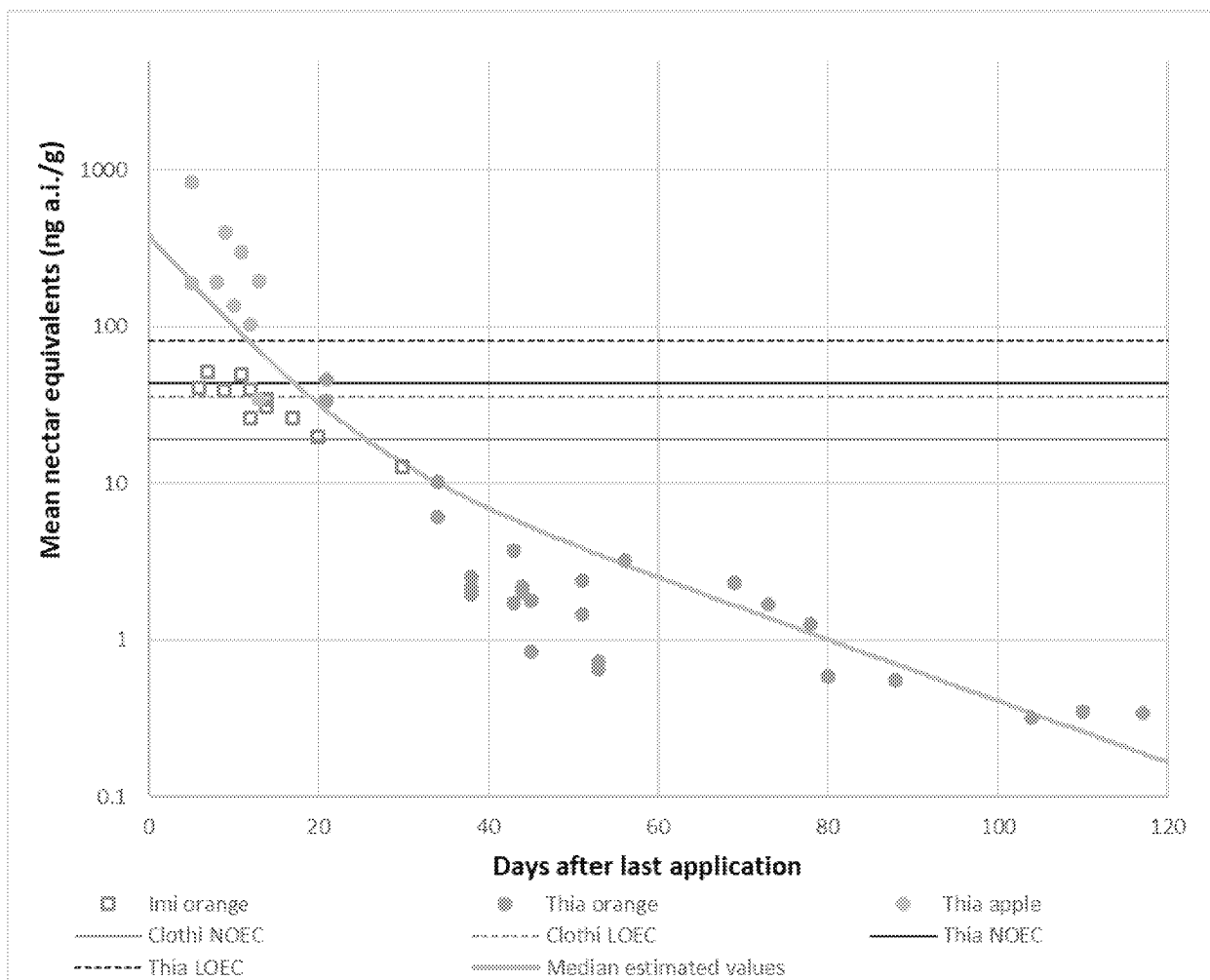


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]2. Measured neonicotinoid residue data in orchard crops (normalized to 0.11 lb c.e./A as clothianidin equivalents; lowest total application rate for orchard crops) from pre-bloom, foliar applications. Also depicted are the clothianidin and thiamethoxam colony level NOAECs and LOAECs. Residues represents nectar equivalents (sum of nectar and adjusted pollen residues). The residue decline curve depicted on this figure (green line) represents the median estimated residues.

Figure 5-13 depicts total residues from post-bloom foliar applications made at 0.22 lb c.e./A. In these studies, applications were made between 140-324 d before bloom. All residues are well below the clothianidin and thiamethoxam NOAECs. This indicates that post-bloom applications of thiamethoxam to orchard crops pose a low risk to honey bee colonies.

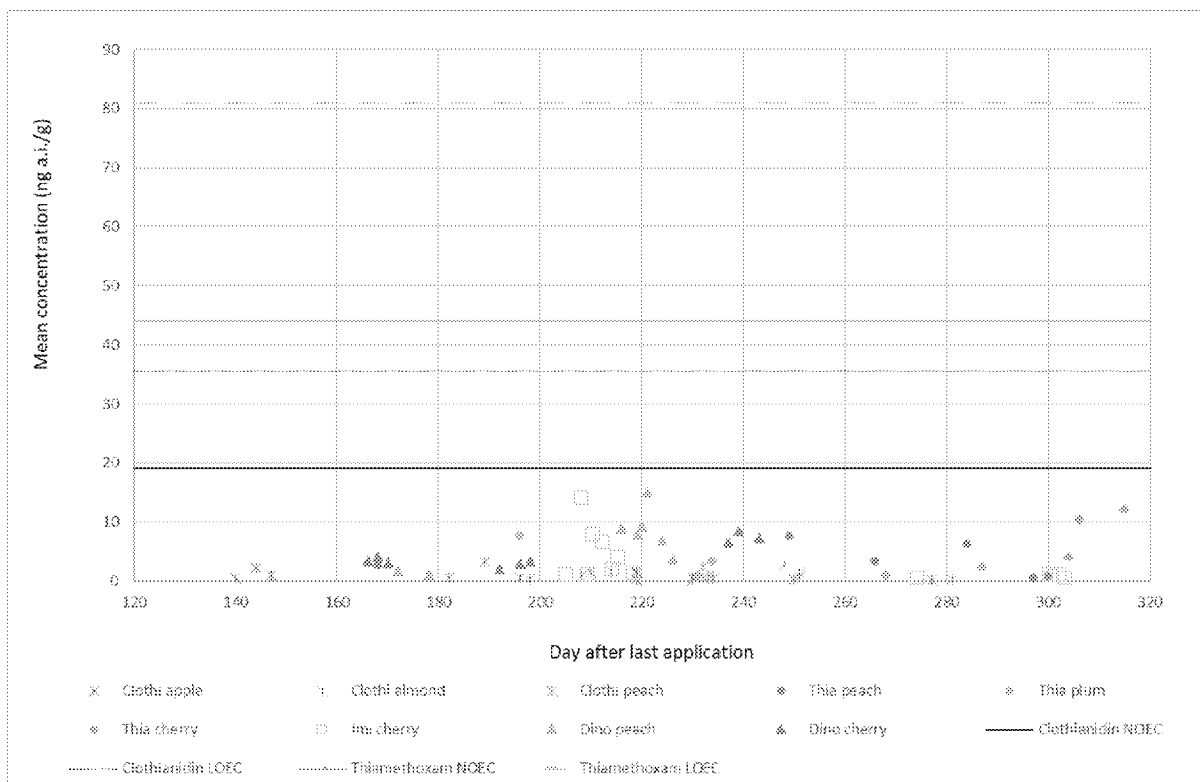


Figure [STYLEREf 1 \s]-13. Measured neonicotinoid residue data in orchard crops (normalized to 0.22 lb c.e./A as clothianidin equivalents) from post-bloom, foliar applications. Also depicted are the clothianidin and thiamethoxam colony level NOAECs and LOAECs. Residues represents nectar equivalents (sum of nectar and adjusted pollen residues).

As discussed previously, there is one orchard field study available with supplemental information. In this study (48584701), thiamethoxam was applied to pears at a rate of 0.085 lb a.i./A, which is above the maximum allowed single application rate for pome fruit (0.074 lb a.i./A) but does not consider that multiple applications of 0.074 lb a.i./A (for a total of 0.22 lb a.i./A) are allowed on the labels. In this study, increased adult mortality was observed in applications made 1, 3 and 5 days before bloom, but not 8 or 11 days before bloom. This study is limited by its design, which included pseudo replication, and observations of bee mortality were based on bee traps, preventing quantification of bees that died away from the hives. Despite these limitations, observations of increased bee mortality for applications made closer to bloom are consistent with the Tier II analysis discussed above.

Thirteen separate incidents of honey bee kills have been reported in association with applications of thiamethoxam to orchard crops (Table 5-26). These incident reports were assigned “probable” or “possible” certainties as they relate to the thiamethoxam applications. Incident reports are available for stone fruit, citrus and pome fruit (including cherries, lemons, pears and unspecified orchards). The majority (12) of the incidents were reported in Washington in 2002, with one incident in CA on lemons reported in 2015. When considering the legality of use, 8 incidents were associated with registered uses; 4 incidents had undetermined legality and 1 incident was a misuse. Many of the reported incident reports also indicated that other insecticides (e.g., chlorpyrifos, abamectin) were also applied on the same orchards where bee kills were observed. Limited information is provided in each incident report. One important piece of information that is missing from each of these reports is the application method (i.e., foliar or soil) and timing relative to bloom. In the incident report involving the lemon orchard

(I027610-001), the application involved Agri-Flex (EPA Reg. #100-1350). This product is registered for foliar applications, so, it is assumed that this incident is associated with foliar applications. Since thiamethoxam is only registered for foliar applications to cherries and to pears, it is assumed that these incidents involved foliar applications. In regard to the incidents involving unspecified orchard crops, since these orchards were located in Washington state, and a low amount of orchard acreage grown in this state is citrus, it is assumed that these incidents involved a crop for which only foliar applications may be made. In summary, it is considered most likely that the reported incidents involving orchards were from foliar applications.

Table [STYLEREf 1 \s]-26. Reported bee incidents in the US involving orchard uses of thiamethoxam.

Incident #	Crop	Legality *	Certainty* *	State	year	Residues* **	Effects
I020998-001	Cherry orchard	R	Ps	WA	2002	NR	Slight to moderate bee kill in 4 hives
I020998-003	Cherry orchard	U	Ps	WA	2002	NR	Bee kill
I027610-001+	Lemon	R	Ps	CA	2015	NR	dead bees observed in 134 of 400 hives
I020998-002	Orchard	M	Pr	WA	2002	NR	slight to moderate bee kill
I020998-004	Orchard (unspecified)	U	Pr	WA	2002	NR	Bee kill
I020998-005	Orchard (unspecified)	U	Pr	WA	2002	NR	Bee kill
I020998-017	Orchard (unspecified)	R	Ps	WA	2002	NR	Bee kill
I020998-018	Orchard (unspecified)	R	Ps	WA	2002	NR	Bee kill
I020998-019	Orchard (unspecified)	R	Ps	WA	2002	NR	Bee kill
I020998-020	Orchard (unspecified)	R	Ps	WA	2002	NR	Bee kill
I020998-021	Orchard (unspecified)	R	Ps	WA	2002	NR	Bee kill
I020998-006	pear orchard	U	Pr	WA	2002	NR	Bee kill
I020998-016	pear orchard	R	Ps	WA	2002	NR	Bee kill

*U=undetermined, R = registered use, M = misuse

**HPr= highly probable, Pr= probable, Ps=possible

***T= thiamethoxam, C= clothianidin, NR = not reported

+Agri-Flex Miticide/Insecticide (EPA Reg. #100-1350)

When considering the different lines of evidence presented above, i.e., residue data compared to CFS endpoints (Tier II), field studies and incident reports, there is strong evidence of risk to honey bee colonies due to foliar applications of thiamethoxam to orchard crops. When considering the residue data, there is a difference in risk based on the timing of the application, relative to bloom, with pre-bloom applications (made within several weeks of bloom) presenting a risk but post-bloom applications

representing a low risk to honey bee colonies. This is further supported by the available Tier III studies, which demonstrated bee kills following foliar applications to orchard crops. An additional line of evidence is the incident data, which report bee kills in 13 incidents. Although limited data are available on the application method, one incident involving lemons likely involved foliar applications. In summary, there is strong evidence of risk to honey bee colonies from pre-bloom foliar applications of thiamethoxam to orchards, and there is low risk from post-bloom foliar applications.

Thiamethoxam: Soil Applications (citrus only)

Available residue studies of soil applications of neonicotinoids to the orchard crops are summarized in **Table 5-27** below. Based on the bridging analysis (**Attachment 2**), the available orchard data are bridged across crop and chemical. As discussed above, thiamethoxam is only registered for soil applications to citrus crops at a maximum rate of 0.15 lb c.e./A (total) **as clothianidin equivalents**. Residue data are available for oranges and lemons treated with thiamethoxam. Since data are bridged across chemicals, the available clothianidin residue data are also used to characterize risks of thiamethoxam to honey bees.

It should be noted that the berry residue data were used in the clothianidin assessment above for a line of evidence. Since thiamethoxam is only registered for use on citrus, and citrus residue data are available, additional lines of evidence are not needed here. Therefore, the berry residue data are not included below.

Figure 5-14 depicts the total residue concentrations (based on residues from nectar and pollen, with pollen adjusted to nectar equivalents by dividing by 20; details provided in **Attachment 1**), adjusted to the maximum soil application rate allowed for thiamethoxam on citrus (*i.e.*, 0.15 lb c.e./A). When considering the proportion of clothianidin and thiamethoxam residues in citrus nectar, residues are on average 30% (range: 28-32%) clothianidin. This indicates that both matrices are relevant to evaluation of the residues. Therefore, the available total residues are compared to the clothianidin and thiamethoxam the colony-level CFS NOAECs and LOAECs (**Figure 5-14**). The following summarizes the residues that exceed the different endpoints:

- One residue (123 ng c.e./g) exceeds (by 1.5x) the thiamethoxam LOAEC (81 ng c.e./g)
- Five residue values (range: 48-123 ng c.e./g), exceed the thiamethoxam NOAEC (44 ng c.e./g)
 - one of which is from a thiamethoxam study;
 - These exposure values are as high as 2.8x the thiamethoxam NOAEC
- Eight residues (range: 37-123 ng c.e./g) exceed the clothianidin LOAEC (35.5 ng c.e./g)
 - These exposure values are as high as 3.5x the clothianidin LOAEC
- Sixteen residues (range 21-123 ng c.e./g) exceed the clothianidin NOAEC (19 ng c.e./g)
 - These exposure values are as high as 6.5x the clothianidin NOAEC

Soil applications are only allowed on citrus. For soil applications, residues exceed the clothianidin and thiamethoxam CFS colony-level NOAEC and LOAEC values for >5 months, which represents both the pre- and post-bloom timing windows. Residue levels are within an order of magnitude of the CFS endpoints. In order to dilute residues below the clothianidin and thiamethoxam NOAECs, bees would need to forage <15% and <31% of their total food from orchards treated with thiamethoxam. Taken together, the lines of evidence represent strong evidence that pre-bloom soil applications present a risk to honey bee colonies. For post-bloom applications, there is a limited number of samples representing post-bloom application timing. Only 2 of the residue values exceed the clothianidin NOAEC; however, none of

the residues exceed the thiamethoxam NOAEC. Therefore, for post-bloom, soil applications of thiamethoxam to citrus, the evidence of risk is weakest.

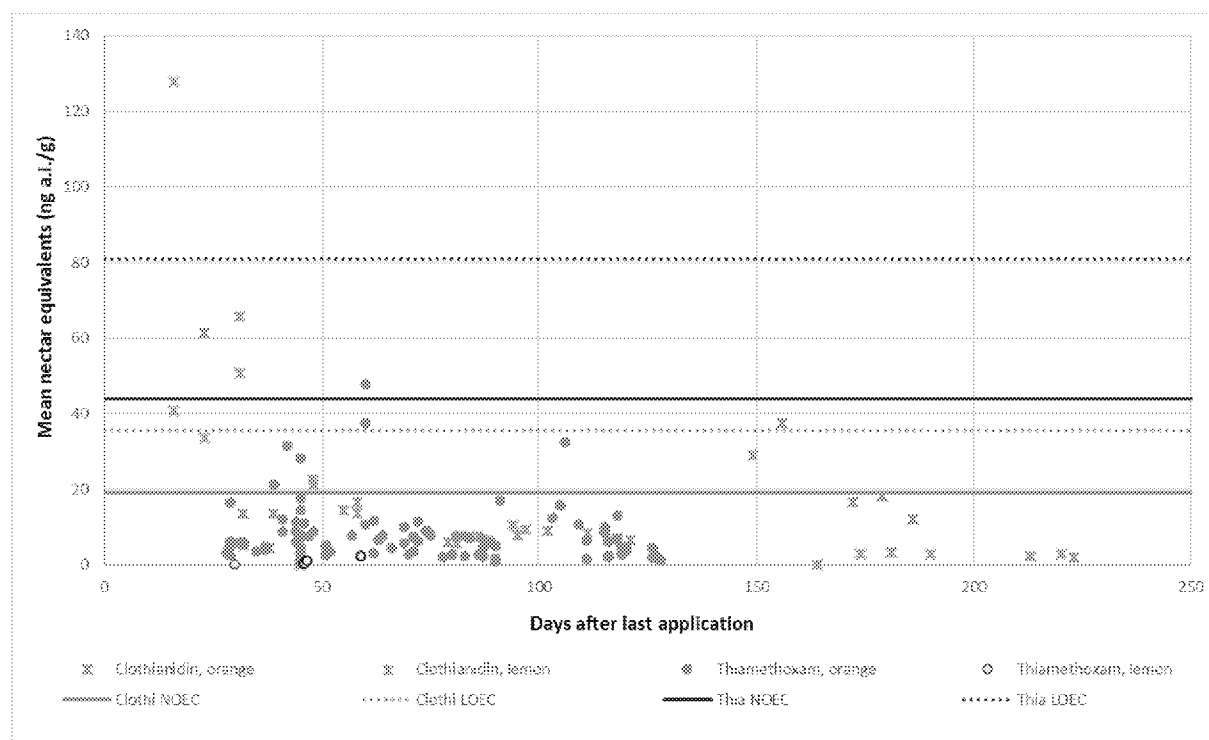


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]4. Measured neonicotinoid citrus residue data expressed as nectar equivalents (sum of nectar and adjusted pollen residues and normalized to 0.15 lb c.e./A as clothianidin equivalents) from soil applications. Also depicted are clothianidin and thiamethoxam colony-level NOAECs and LOAECs.

5.2.2.4 Berries and Small Fruits

The berry and small fruit crop group (13-07) contains a diverse group of commodities, including bushberries (*e.g.*, blueberry), caneberries (*e.g.*, raspberry), large shrubs and trees (*e.g.*, elderberry), climbing vines (*e.g.*, grape), and low growing berries (*e.g.*, strawberry). According to the USDA guidance on crops attractive to honey bees and other bees (USDA 2017), the majority of berry and small fruit crops are considered attractive to honey bees. In addition, many berries require pollination by bees and utilize managed pollinators. One notable exception is grapes, which does not require bee pollination and only produces bee attractive pollen.

For foliar applications (**Table 5-27**), clothianidin is only registered for use on berries (including bushberries, low growing berries and grapes) at maximum rates of 0.067 lb c.e./A (x3 applications) and 0.1 lb c.e./A (x2 applications), respectively. Grapes are registered for soil and foliar application uses at maximum applications rates of 0.1 and 0.2 lbs c.e. respectively. The maximum seasonal rate allowed is 0.2 lbs c.e./A which allows for 2 foliar applications. Clothianidin is also registered on blueberry for post bloom foliar applications for which no usage data are available. These rates for foliar applications are less at 0.07 lb a.i./A and are at 0.2 lb c.e./A for soil with a maximum of 0.2 lb of c.e./A per season.

For thiamethoxam (**Table 5-27**), thiamethoxam is registered for foliar use on caneberries, bushberries, small fruit climbing vines (including grape), strawberries and low growing berries and for soil use only on bushberries, grapes and strawberries. The maximum foliar application rate is 0.053 lbs c.e./A with 3 applications while the maximum soil application rate is a single 0.23 lb c.e./A application.

Table [STYLEREf 1 \s]-27. Foliar and soil application rates (in lb c.e./A) and number of applications (x n) for clothianidin and thiamethoxam on berry crops (based on current labels). Thiamethoxam rate expressed as clothianidin equivalents.

Subgroup/crop	Subgroup ID	Clothianidin		Thiamethoxam	
		Foliar	Soil	Foliar	Soil
Caneberries	13-07A	NR	NR	0.040 (x2)	NR
Bushberries	13-07B	0.067 (x3)*	0.2 (x1)*	0.053 (x2)	0.16 (x1)
Large shrub/tree	13-07C	NR	NR	NR	NR
Small fruit climbing vines	13-07D	NR	NR	NR	NR
Small fruit climbing vines (except grape)	13-07E	NR	NR	0.047 (x2)	NR
Small fruit climbing vines (except kiwifruit)	13-07F	NR	NR	NR	NR
Grapes	NA	0.1 (x2)	0.2 (x1)	0.048 (x2)	0.23 (x1)
Low growing berries	13-07G	NR	NR	NR	NR
Strawberries	NA	NR	NR	0.053 (x3)	0.16 (x1)
Low growing berries (except strawberry)	13-07H	0.067 (x3)*	0.2 (x1)*	0.053 (x2)	NR

*post-bloom only

NR = not registered

NA = not applicable

Of the registered berry uses of clothianidin, usage data are only available for grapes, with 2,000 lbs applied annually (**Table 5-28**). Specific to thiamethoxam, the majority of use is on grapes and strawberries, with an average of 1,000 pounds applied annually per crop. Other thiamethoxam usage information is available for blueberries and caneberries (**Table 5-28**).

Table [STYLEREf 1 \s]-28. Screening-Level Use Assessment (SLUA) data for applications of clothianidin and thiamethoxam to berry and small fruits.

Crop	Clothianidin			Thiamethoxam		
	Average Lbs. A.I. Applied per Year	Percent Crop Treated		Average Lbs. A.I. Applied per Year	Percent Crop Treated	
		Average	Maximum		Average	Maximum
Grapes	2,000	<2.5	5	1,000	<2.5	5
Strawberries	NA	NA	NA	1,000	20	40
Caneberries	NA	NA	NA	<500	15	25
Blueberries	NA	NA	NA	<500	<2.5	<2.5

NA = not available

For clothianidin, post-bloom foliar applications to berry crops and soil applications (pre and post bloom) represent a low risk to honey bee colonies. This is based on the observation that measured

residues from grapes and blueberries are all below the clothianidin CFS NOAEC. **For pre-bloom foliar applications to grapes, there is strong evidence of risk to honey bee colonies foraging on treated vineyards.** Residue data from grapes treated with clothianidin are above the NOAEC and LOAEC. The maximum measured sample represents 29% and 54% of the NOAEC and LOAEC, respectively, suggesting that bees could forage for roughly 1/3-1/2 of their pollen needs (grapes only produce pollen) on treated vineyards and still potentially manifest colony effects. The lines of evidence for the clothianidin risk conclusions are summarized in **Table 5-29** and discussed below.

For thiamethoxam, post-bloom foliar and soil applications to berry crops represent a low risk to honey bee colonies. This is based on the observation that measured residues from grapes and blueberries are all below the clothianidin CFS NOAEC. For foliar pre-bloom applications, residues dissipate to below the CFS endpoints before times that would represent post-bloom timing of application. **For pre-bloom foliar and soil applications to berries, there is strong evidence of risk to honey bee colonies foraging on treated fields.** Residue data from multiple crops following pre-bloom foliar and soil applications are above the thiamethoxam CFS NOAEC and LOAEC values. The lines of evidence for the thiamethoxam risk conclusions are summarized in **Table 5-30** and discussed below.

Table [STYLEREf 1 \s]-29. Lines of evidence considered in risk call for applications of clothianidin to the berry and small fruit crop group.

Line of evidence		Foliar applications, pre-bloom (Strong Evidence of Risk)		Foliar applications, post-bloom (LOW Risk)		Soil applications, pre-bloom (LOW risk)		Soil applications, post-bloom (LOW risk)	
Clothianidin specific residue data		Grape		Grape		Grape		None	
Residue data for other chemicals		None (grape is only registered use)		None		None (grape is only registered use)		Imidacloprid (Blueberry)	
Measured Data:	Exceedance Attribute	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC	LOAEC
	Frequency: Number daily mean residue values > NOAEC & LOAEC	4	3	None	None	None	None	None	None
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	37	37	None	None	None	None	None	None
	Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	3.4x (29%)	1.8x (54%)	0.05x (not calculated)	0.03x (not calculated)	0.4x (not calculated)	0.2x (not calculated)	0.1x (not calculated)	0.05x (not calculated)
Crop Attractiveness ⁽²⁾ & Bloom Duration		Blueberries (registered for post-bloom applications only): Nectar and pollen are attractive to honey bees Grapes: Only pollen is attractive to honey bees. Bloom duration varies depending on crop/variety.							
Managed Pollinators		Blueberries: Yes Currants and gooseberries require bee pollination; however, managed pollinators are not used Grapes do not require bee pollinators nor use managed pollinators							
Ecological Incidents		None reported							
Spatial extent of risk (annual acres treated)		Grapes: <24,100 (ave), <48,100 (max)							

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]0. Lines of evidence considered in risk call for applications of thiamethoxam to berries.

Line of evidence		Foliar applications (Strong Evidence of Risk)				Foliar applications, post-bloom (LOW Risk)		Soil applications, pre-bloom (Strong evidence of risk)				Soil applications, post-bloom (Low risk)	
Thiamethoxam specific residue data		Blueberry, cranberry, strawberry				None		Strawberry				None	
Crop-specific residue data for other chemicals		Dinotefuran: blueberry and cranberry; Clothianidin: grape				Clothianidin grape		Clothianidin grape				imidacloprid Blueberry	
Percent of clothianidin present in total residues		Cranberry: 1-18 Strawberry: 0.1-8 Blueberry: 4-92				Not available		1-60				Not available	
Measured Data:	Exceedance Attribute	Clothi NOAEC	Clothi LOAEC	Thia NOAEC	Thia LOAEC	Clothi NOAEC	Thia NOAEC	Clothi NOAEC	Clothi LOAEC	Thia NOAEC	Thia LOAEC	Clothi NOAEC	Thia NOAEC
	Frequency: Number daily mean residue values > NOAEC & LOAEC	39	37	37	26	None	None	14	10	10	4	None	None
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	23	22	22	15	None	None	83	83	83	83	None	None
	Magnitude: Ratio of Max to NOAEC & LOAEC (% of diet required to reach NOAEC & LOAEC)	52x (1.9%)	28x (3.6%)	23x (4.4%)	12x (8.1%)	0.03x (not calculated)	0.01x (not calculated)	8.0x (13%)	4.3x (23%)	3.5x (29%)	1.9x (53%)	0.05x (not calculated)	0.02x (not calculated)
Modeled Data: (90 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	29	24	22	18	Not applicable							
	Magnitude: Ratio to Max to NOAEC & LOAEC (% of diet required to reach NOAEC & LOAEC)	128x (0.8%)	68x (1.5%)	55x (1.8%)	30x (3.3%)								
Modeled Data: (70 th percentile)	Duration: Max Interval (d) since	24	20	18	14								

Line of evidence		Foliar applications (Strong Evidence of Risk)				Foliar applications, post-bloom (LOW Risk)	Soil applications, pre-bloom (Strong evidence of risk)	Soil applications, post-bloom (Low risk)
	application with NOAEC/LOAEC exceedance							
	Magnitude: Ratio to Max to NOAEC & LOAEC (% of diet required to reach NOAEC & LOAEC)	53x (1.9%)	28x (3.5%)	23x (4.4%)	12x (8.1%)			
Modeled Data: (50 th percentile)	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	21	17	16	12			
	Magnitude: Ratio of Max to NOAEC & LOAEC (% of diet required to reach NOAEC & LOAEC	29x (3.4%)	16x (6.4%)	13x (7.9%)	6.9x (14.6%)			
Crop Attractiveness*& Bloom Duration		Blueberries, cranberries, raspberries, strawberries: Nectar and pollen are attractive to honey bees Currants and gooseberries: Only nectar is attractive to honey bees Grapes: Only pollen is attractive to honey bees. Bloom duration varies depending on crop/variety.						
Managed Pollinators		Blueberries, cranberries, raspberries: Yes Strawberries do not require bee pollinators; however, managed pollinators are used Currants and gooseberries require bee pollination; however, managed pollinators are not used Grapes do not require bee pollinators nor use managed pollinators						
Ecological Incidents		None reported						
Spatial extent of risk (annual acres treated)		Blueberries: <1,900 (ave and max) Caneberries: 2,600 (ave), 4,300 (max) Grapes: <24,000 (ave), 48,000 (max) Strawberries: 12,000 (ave), 23,000 (max)						
Other considerations		For foliar pre-bloom applications, residues dissipate to below the CFS endpoints before times that would represent post-bloom timing of application. This supports the low risk conclusion.						

*Based on USDA 2017

Another consideration of the risk potential is the spatial extent of risk. As discussed previously, usage data are available for clothianidin applications to grapes and thiamethoxam on blueberries, grapes, strawberries and caneberries. The number of acres treated based on SLUA data (PCT) and acres grown (USDA 2017) is presented in **Table 5-31** for each chemical. When the total number of acres of berries (for which usage data are available) is considered, this translates to an annual average of <2,930 acres treated with clothianidin and 14,200-40,200 acres treated with thiamethoxam. When considering the maximum annual PCT data for usage, as much as 5,860 acres of berries are estimated to be treated with clothianidin and 77,600 acres treated with thiamethoxam.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]1. Estimated annual acres treated for clothianidin and thiamethoxam use on berries.

Crops	Clothianidin		Thiamethoxam	
	Average	Max	Average	Max
Blueberries	NA	NA	<1,940	<1,940
Caneberries	NA	NA	2,600	4,330
Grapes	<2,930	5,860	<24,100	48,100
Strawberries	NA	NA	11,600	23,300
Total	<2,930	5,860	40,200	77,600

Clothianidin: Foliar, pre-bloom applications

Clothianidin-specific data are available for pre-bloom applications to grapes (MRID 50154305). Since grapes is the only registered foliar use allowed for pre-bloom applications, and the bridging analysis (**Attachment 2**) indicated a difference in the magnitude of residues between berry crops, no other residue data need be considered here. The available clothianidin grape residue data are presented in **Figure 5-15** for pre-bloom and **Figure 5-16** for post-bloom foliar applications, along with colony-level NOAEC and LOAEC from the available CFS. Values were normalized to the maximum single application rate registered for grapes (*i.e.*, 0.1 lb c.e./A). As discussed above, grapes only produce pollen, therefore, these residues represent concentrations measured in pollen, with adjustment to nectar-equivalents (*i.e.*, mean residues are divided by 20). Nectar-equivalent residues from pre-bloom foliar applications of clothianidin to grapes range from 14 to 65 ng c.e./g, with 4 values above the colony-level NOAEC and 3 above the LOAEC. Residues exceed the clothianidin CFS LOAEC for at least 37 days after last application.

Grape is the only registered pre-bloom use on berries for clothianidin. Since grapes only produce pollen, this is the only matrix of interest for this crop. Residues in pollen of grapes were higher than other berry crops, preventing bridging of residues from pollen of other berry crops to grapes. The available clothianidin grape data set is limited in number of samples collected, which prevents a suitable fit of the dissipation of the residues over time. Therefore, a reliable Monte Carlo analysis could not be conducted for this use. Since there are residue data available for clothianidin applications to grapes, the lack of a Monte Carlo analysis does not represent a limitation for the risk conclusions.

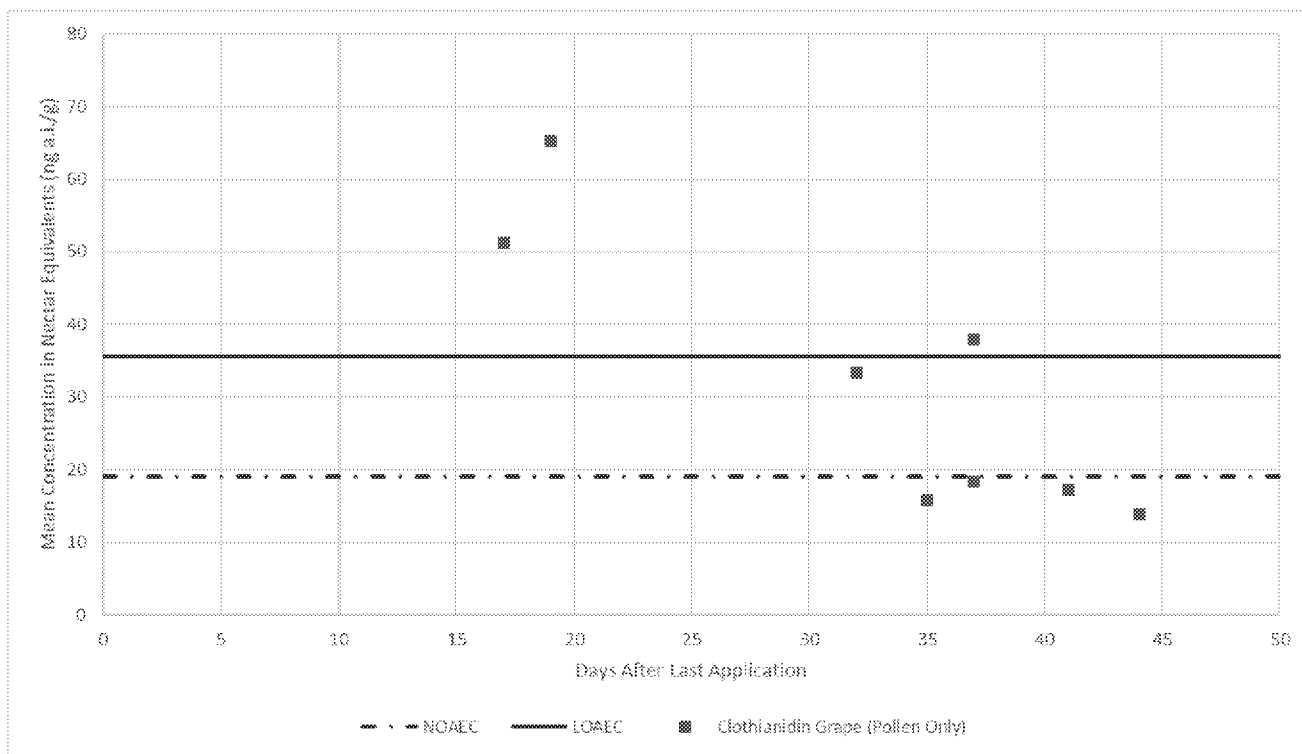


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]. Measured clothianidin residues, based on pollen alone and expressed in nectar equivalents (normalized to maximum single application rate of 0.1 lb c.e./A) in grape (pre-bloom foliar) versus the clothianidin endpoint overlaid on colony-level NOAEC and LOAEC values. Bars represent the 95% confidence intervals.

The maximum measured daily mean value (normalized to the maximum single application rate of 0.1 lb c.e./A) was 65 ng c.e./g. At this concentration, 29% of diet would need to come from the treated area to reach the clothianidin CFS NOAEC, while 54% of the diet would need to come from the treated area to reach the clothianidin CFS LOAEC, suggesting that dilution of the overall clothianidin concentration in food by uncontaminated pollen and nectar sources may not result in an exposure below effect levels. Based on this analysis, there is strong evidence for risk to honey bee colonies feeding on grape vineyards receiving foliar, pre-bloom treatments of clothianidin.

Clothianidin: Foliar, post-bloom Applications

As discussed above, clothianidin is registered for post-bloom foliar applications to grapes, bushberries and low growing berries (except strawberry). Of those subgroups/crops, residue data are only available for post-bloom applications to grapes (MRID 50154305). As with the pre-bloom foliar residue grape data from the same study (discussed above), pollen residue data were adjusted to nectar equivalents and are depicted in **Figure 5-16**. Also depicted in this figure is the clothianidin CFS NOAEC. All residues are below the NOAEC.

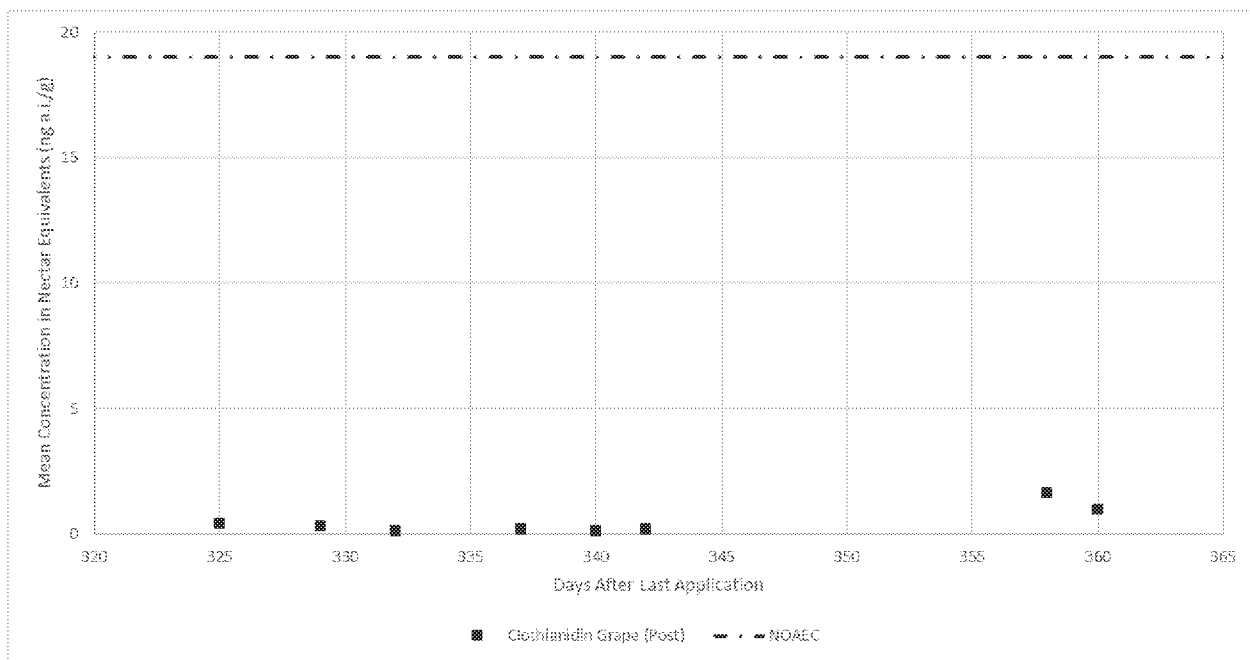


Figure [STYLEREf 1 \s]-[SEQ Figure * ARABIC \s 1]6. Measured clothianidin residues based on pollen alone expressed in nectar equivalents (normalized to the maximum single application rate of 0.1 lb c.e./A) in grape (post-bloom foliar) versus the clothianidin colony-level NOAEC.

There are some uncertainties in the available data due to timing of when the samples were collected (i.e., 325 days or more after application). If post-bloom applications may occur sooner, the magnitude of those residues is unknown. Considering this, as well as the registered foliar post-bloom use on other berry crops that have both honey bee attractive pollen and nectar (*e.g.* blueberry), the full dataset for neonicotinoid residues in berry crops was considered. For foliar pre-bloom applications (**Figure 5-17**), residues dissipate to below the CFS endpoints in approximately 2 months. It is assumed that post-bloom applications would occur with more than 2 months before the next flowering cycle. Therefore, the dissipation of residues from pre-bloom applications suggests that residues measured from post-bloom applications will be below CFS endpoints. Therefore, a low risk conclusion is made for post-bloom foliar applications of clothianidin to berries.

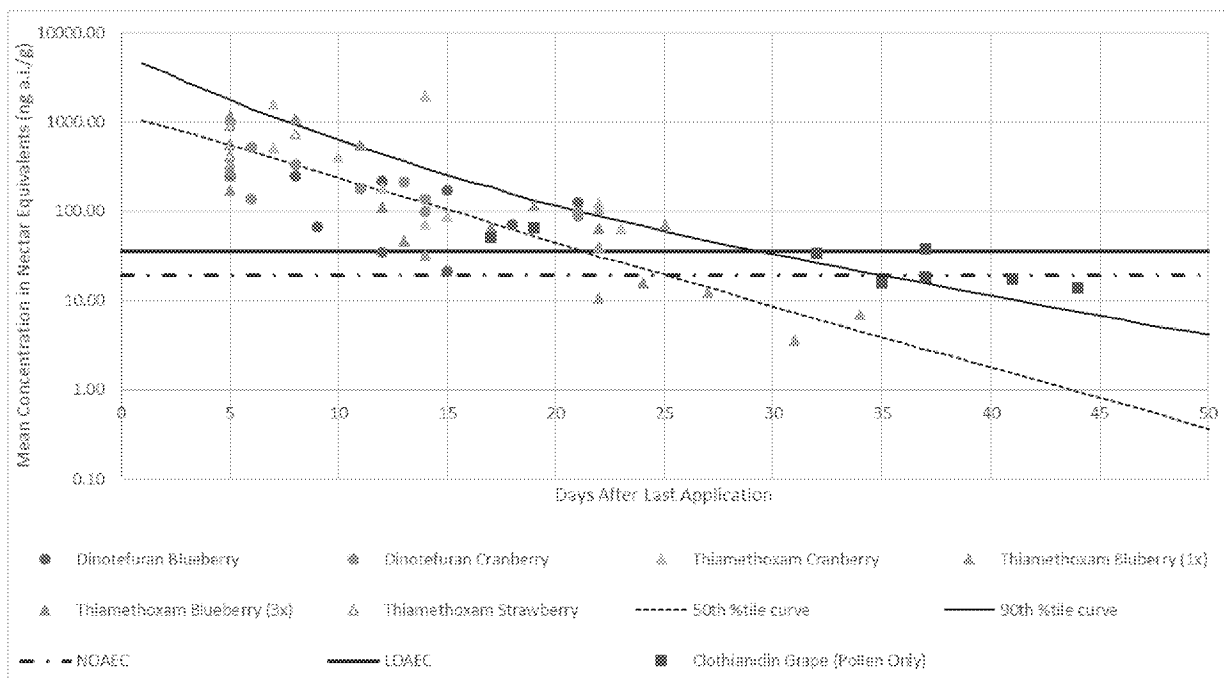


Figure [STYLeref 1 \s]-17. Measured neonicotinoid berry floral residues expressed in nectar equivalents (normalized to maximum single application rate of 0.1 lb c.e./A) versus the clothianidin colony-level NOAEC and LOAEC.

Clothianidin: Soil, pre-bloom Applications

As with foliar applications, grape is the only crop of the berry group where pre-bloom soil applications are allowed. Pre-bloom residue data are available for grapes (MRID 50154305) and are depicted in **Figure 5-18**. This figure depicts pollen residue data adjusted to nectar equivalents (as discussed above, grapes do not produce honey bee attractive nectar). Measured residues in grape pollen for clothianidin are consistently below both the colony-level NOAEC and LOAEC values. Therefore, a low risk conclusion is made for pre-bloom soil applications of clothianidin to grapes.

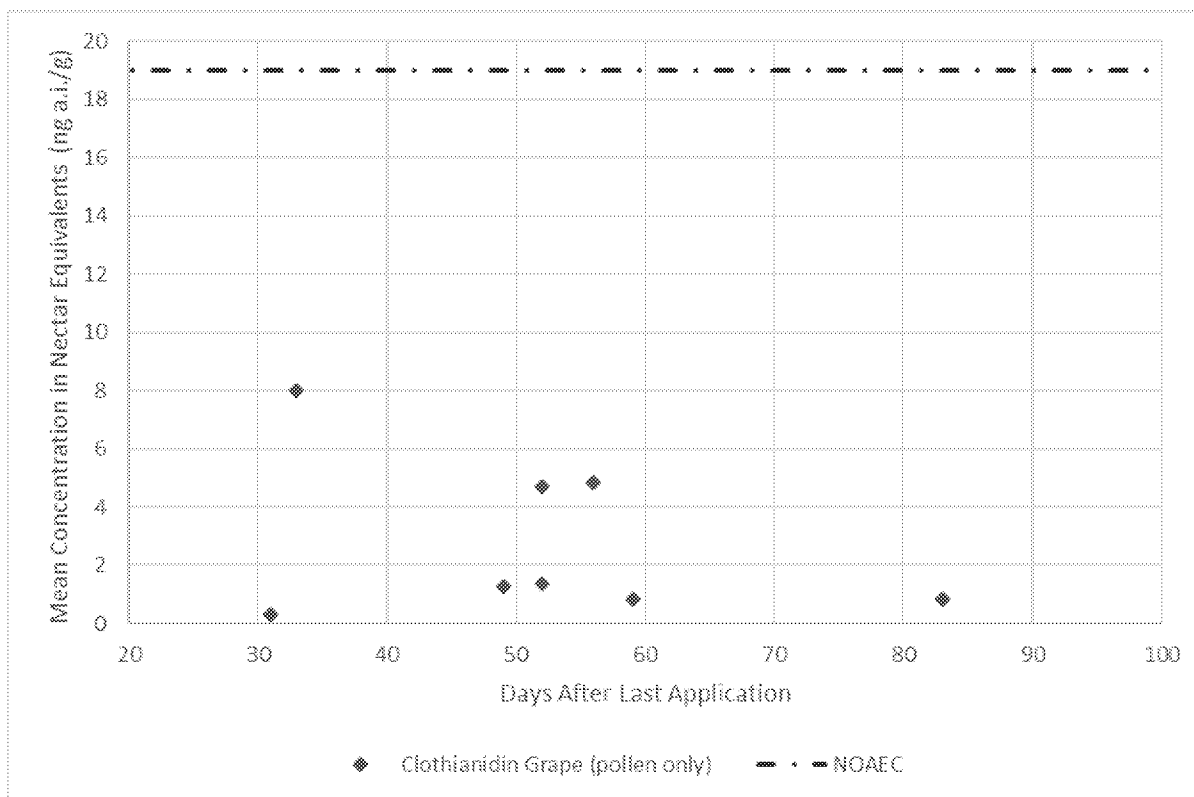


Figure [STYLERE 1 \s]-18. Measured clothianidin residues expressed in nectar equivalents (normalized to the maximum single application rate of 0.2 lb c.e./A) in grape (pollen only) versus the clothianidin endpoint.

Clothianidin: Soil, post-bloom Applications

As discussed above, clothianidin is registered for post-bloom soil applications to grapes, bushberries and low growing berries (except strawberry). Of those subgroups/crops, neonicotinoid residue data are only available for post-bloom imidacloprid applications to blueberries (MRID 49535602). When normalized to the clothianidin maximum single and seasonal application rate (0.2 lb c.e./A), the residue values are below the clothianidin CFS NOAEC endpoint (**Figure 5-19**). This suggests low risk to honey bee colonies.

As discussed above, there is some uncertainty in this risk call due to the timing of the samples (i.e., collected 228 d or more before bloom). If post-bloom applications are carried out closer to bloom (of the following year), there is potential that residues will be higher; however, they would need to be at least an order of magnitude greater to pose a risk to colonies.

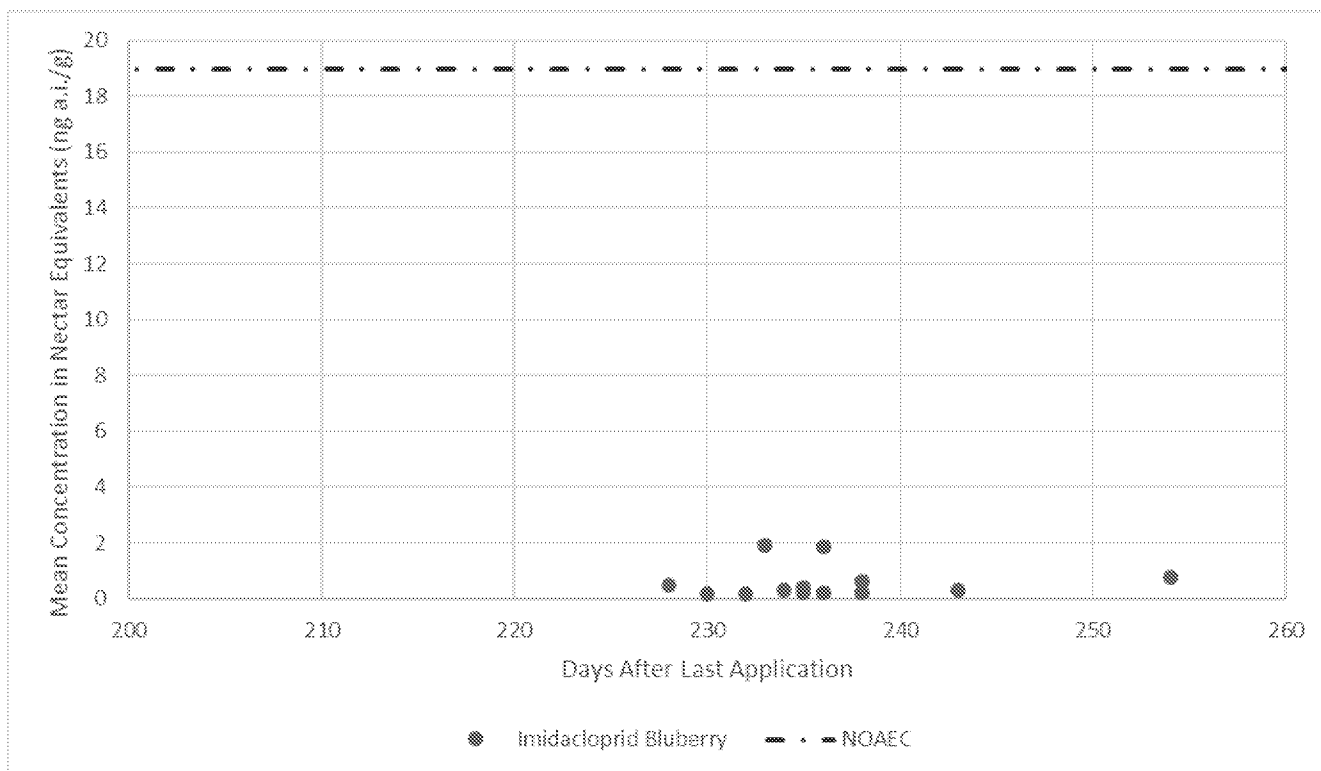


Figure [STYLEREf 1 \s]-19. Mean-measured residues expressed in nectar equivalents (normalized to the maximum single and seasonal application rate of 0.2 lb c.e./A) in blueberry from post-bloom soil applications of imidacloprid versus the clothianidin colony-level NOAEC and LOAEC.

Thiamethoxam: Foliar, pre-bloom applications

Thiamethoxam is registered for foliar applications to all the berry subgroups, except for large shrubs and trees. Pre- and post-bloom applications are allowed on all berry crops. Thiamethoxam-specific data are available for pre-bloom applications to blueberry (MRID 50425901), cranberry (MRID 49804102), and strawberry (MRID 50265502). For pre-bloom foliar applications, the residue bridging analyses (**Attachment 2**) suggest that crop may have an influence on residue concentrations, while chemical does not have an influence. This is primarily based on similar concentrations across chemical and matrix (*e.g.*, pollen and nectar) for blueberry and cranberry; however, grape concentrations are substantially higher (2-3 orders of magnitude) at comparable sampling intervals. Therefore, residue data for other chemicals (dinotefuran blueberries, MRID 50145707; dinotefuran cranberries, MRID 49841002 and clothianidin grape, MRID 50154305) are considered here.

Based on the bridging analysis conclusions, the thiamethoxam and dinotefuran blueberry and cranberry data are bridged across all chemicals and used to represent crops in the low-growing berry subgroups (13-07G and H). For the small fruit vine climbing subgroups (13-07D and 13-07F), the only data available are for clothianidin residues in grape pollen. It is uncertain how representative residues in grape pollen are for other nectar producing crops in the small fruit climbing subgroups.

Thiamethoxam and clothianidin were both detected in pollen and nectar samples collected from berries treated with thiamethoxam. In the blueberry study, clothianidin represented 4-62% of the total residue in pollen and 33-92% in nectar. In cranberries and strawberries, the proportion of clothianidin was much

less, ranging 1-18% in cranberry pollen, 1-8% in strawberry pollen, 2-12% in cranberry nectar and 0.1-5% in strawberry nectar. This suggests that the proportion of clothianidin present in nectar and pollen may vary by crop and that the endpoints for both chemicals are relevant; however, the clothianidin endpoints may be more relevant for some crops (*e.g.* blueberry) than others (*e.g.*, strawberry and cranberry).

Monte Carlo distributions for the bushberry and low-growing berry subgroups representing the 50th and 90th percentiles of the data are presented in **Figure 5-20**, along with the measured residue data and the colony-level NOAEC from the available CFS. Residue values were normalized to the maximum single application rate registered across the low-growing berry subgroup (*i.e.*, 0.053 lb c.e./A). Predicted residues based on the 90th percentile curves exceed the thiamethoxam NOAEC and LOAEC values for up to 22 and 18 days, respectively (**Table 5-30**). Predicted residues based on the 50th percentile curves exceed the thiamethoxam NOAEC and LOAEC for up to 16 and 12 days, respectively. Considering the proportion of clothianidin residues relative to thiamethoxam residues in berry pollen and nectar (up to 92% described in the blueberry study above), the predicted residues based on the 90th percentile curves exceed the clothianidin CFS NOAEC and LOAEC values for up to 29 and 24 days, respectively. Mean-measured residues from pre-bloom foliar applications of neonicotinoids to berry and small fruit crops range from 1 to 997 ng c.e./g, with multiple values above the NOAEC and LOAEC (**Table 5-30**).

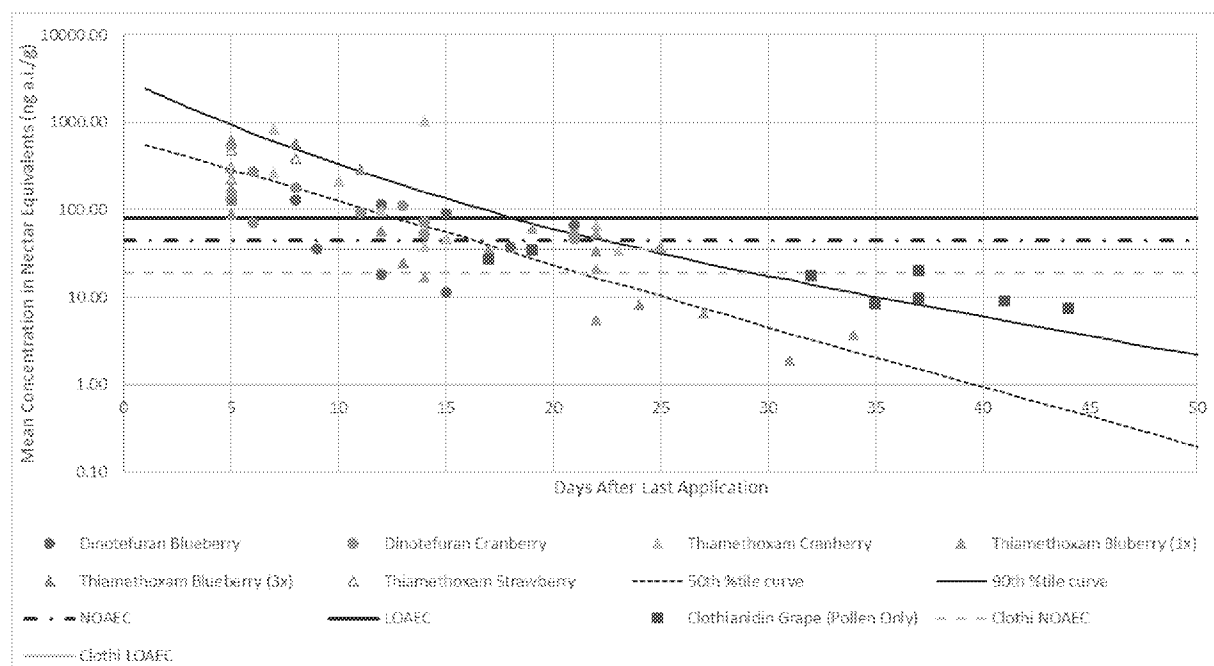


Figure [STYLERE1 1 \s]-[SEQ Figure * ARABIC \s 1]0. 50th and 90th percentile Monte Carlo distributions and measured neonicotinoid residue data (normalized to the maximum single application rate of 0.053 lb c.e./A) versus thiamethoxam NOAEC and LOAEC endpoints for the low-growing berry subgroup. Points represent empirical residues.

For the small fruit vine climbing (*e.g.*, grapes) subgroups, **Figure 5-21** depicts the mean-measured residues from pre-bloom foliar applications of clothianidin to grapes. Values range in grapes from 7 to 31 ng c.e./g (adjusted to the thiamethoxam application rate of 0.048 lb c.e./A). All measured residues

are below the thiamethoxam NOAEC and LOAEC; however, two residues exceed the clothianidin NOAEC. This suggests potential concern for colony level effects. Given the high proportion of clothianidin residues, relative to thiamethoxam residues, in some of the empirical residue studies in berry's (*i.e.* the blueberry study described above), the clothianidin endpoints are considered relevant.

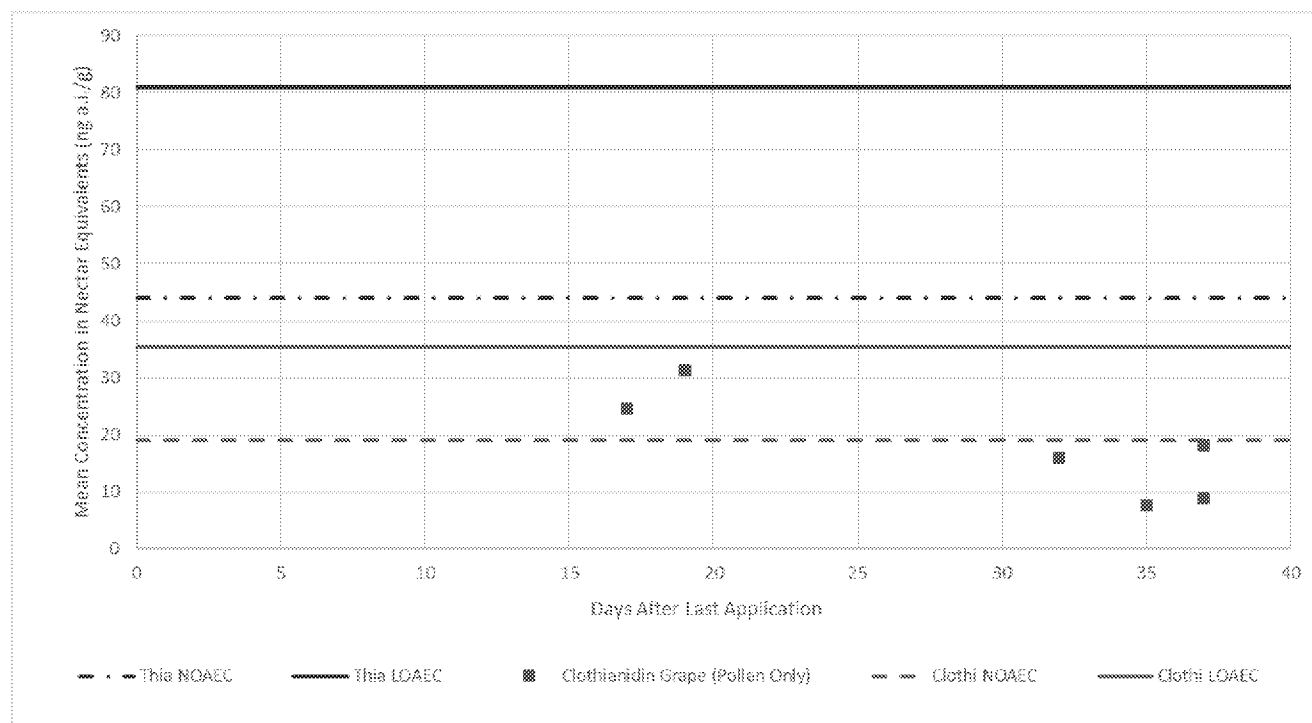


Figure [STYLERE 1 \s]-21. Measured clothianidin residues in grape pollen, expressed in nectar equivalents (normalized to 0.048 lb c.e./A) in grape versus the thiamethoxam endpoint. Lines are the 95% confidence intervals.

No empirical residues are available for caneberries; however, available residues for other berries will be used to assess risks from this subgroup. Given that empirical residues for bushberries, low growing berries and vines exceed colony level endpoints, there is strong evidence of risk to colonies for pre-bloom foliar applications of thiamethoxam.

Thiamethoxam: Foliar, post-bloom applications

Post bloom, foliar applications of thiamethoxam may be made to berries (**Table 5-27**). Only one post-bloom foliar residue study is available (applications of clothianidin to grapes, MRID 50154305). These residue data are considered here (**Figure 5-22**). When comparing the residues to the thiamethoxam and clothianidin colony level endpoints, residues are all below the colony level endpoints. As discussed above (for clothianidin post-bloom foliar applications), there is uncertainty with the timing of the sampling of the available residue data. If we consider the dissipation of the pre-bloom foliar application data (**Figure 5-20**, above), residues will be below colony level endpoints in approximately 1 month. Since post-bloom applications are expected to occur well before 1 month before bloom of the following berry crop, this indicates that post-bloom foliar residues will be below CFS endpoints. This indicates low risk of colony level effects.

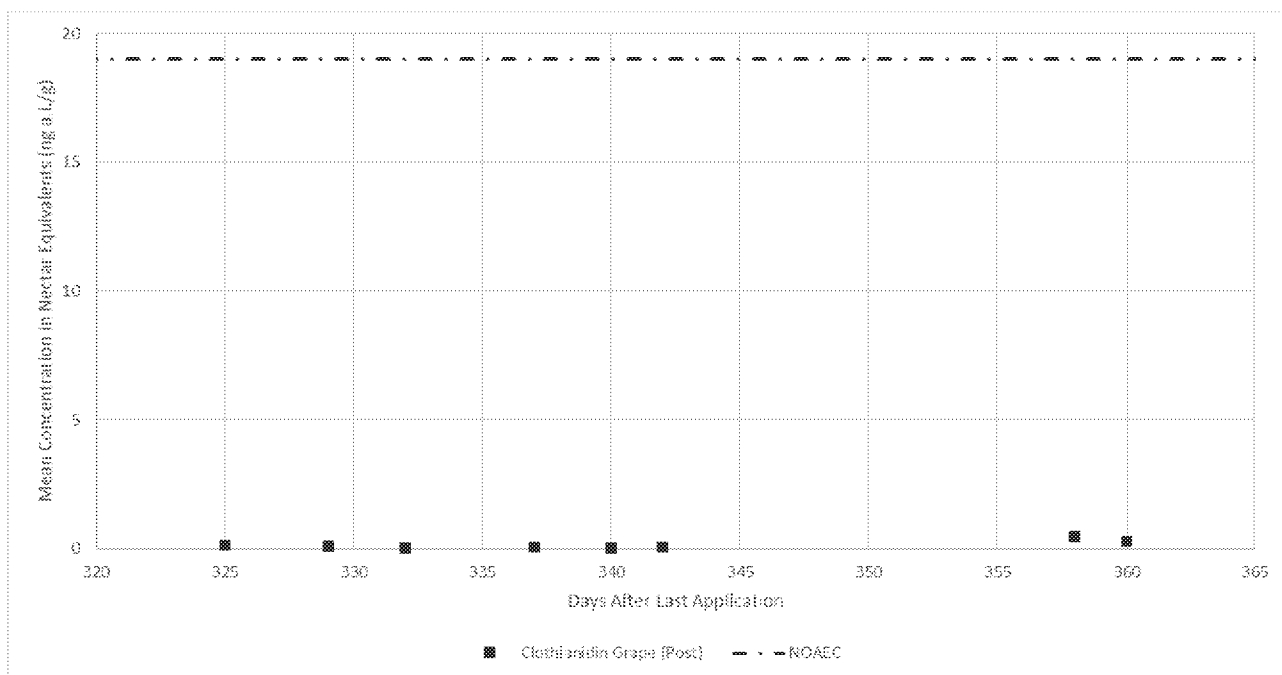


Figure [STYLeref 1 \s]-22. Measured clothianidin residues based on pollen alone expressed in nectar equivalents (normalized to maximum single application rate of 0.053 lb c.e./A) in grape (post-bloom foliar) versus the clothianidin colony-level NOAEC.

Thiamethoxam: Soil, pre-bloom applications

Thiamethoxam is registered for soil applications to bushberries, climbing vines and low growing berries. Thiamethoxam-specific data are available for strawberries (MRID 50266001). In the thiamethoxam study, clothianidin represented 1-60% of total residues in pollen and 1-30% in nectar (indicating that both endpoints are relevant for the risk assessment). Residue data are also available for clothianidin applications to grapes (MRID 50154305). It is noted again, that grape data are for pollen only, and several crops within the small fruit vine (grapes) climbing subgroups also produce nectar (*e.g.*, gooseberries), so it is uncertain how representative residues in grape pollen are for other crops in the subgroups. Data are considered for berry and small fruit crops, *e.g.*, strawberry, and orchard crops to characterize risk from soil applications to berries.

While a Monte Carlo analysis involving residue data and dissipation rate constants was conducted for foliar applications to the fruit and berry crop group, this approach was not supported for soil applications due to limitations in the dataset (**Attachment 2**).

Figures 5-23 and 5-24 present the mean-measured residues from pre-bloom soil applications of neonicotinoids to berries, normalized to the maximum single and seasonal rates for climbing vines (0.23 lb c.e./A) and bushberries and low growing berries (0.16 lb c.e./A). For strawberry and grape, the normalized residues are 218 ng c.e./g for climbing vines and 152 ng c.e./g for bushberries and low growing berries. These residues are an order of magnitude above the colony level endpoints and represent 9 and 13% of the clothianidin colony level endpoint. When the available orchard (citrus), pre-bloom soil application data are normalized to the maximum application rates allowed for berries (*i.e.*,

0.23 and 0.16 lb c.e./A), residues exceed all four thiamethoxam and clothianidin colony level endpoints (Figures x and x). When the available berry and orchard residue data are considered relative to colony level endpoints, the exceedances of colony level endpoints indicate strong evidence of risk to honey bee colonies from pre-bloom soil applications to berries.

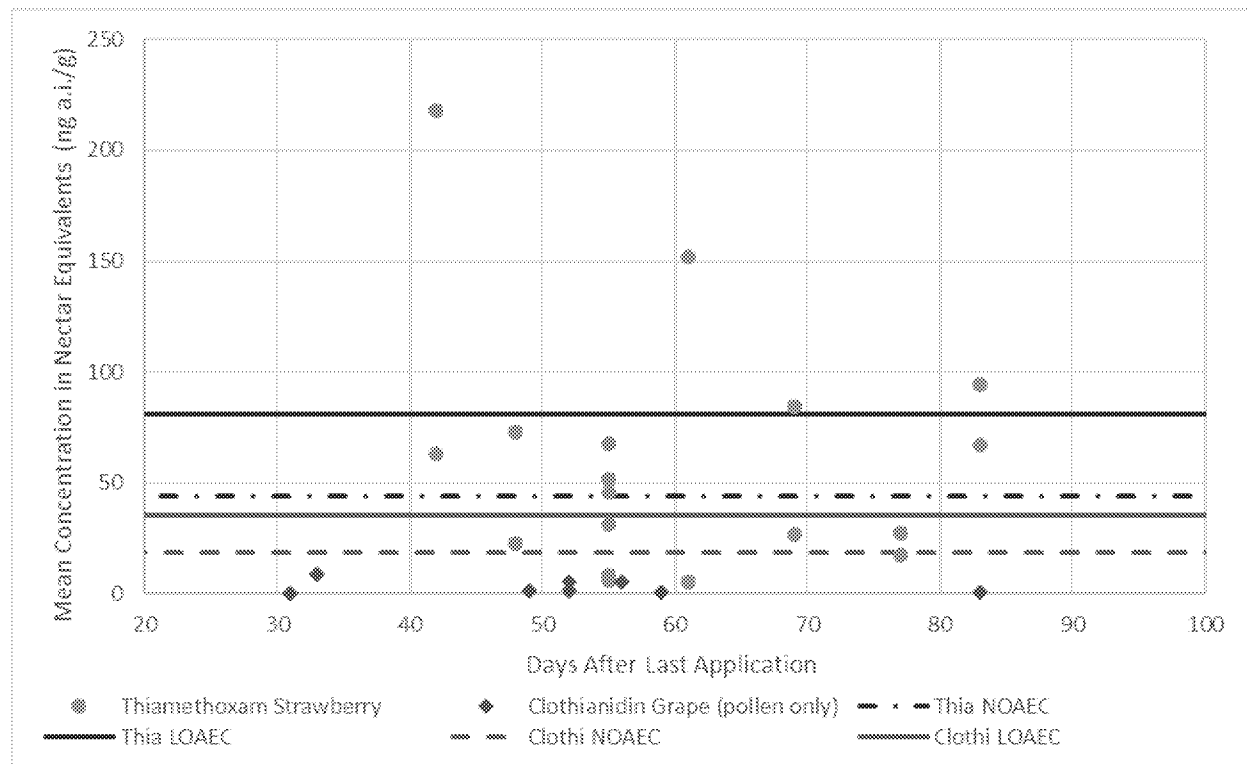


Figure [STYLEREf 1 \s]-23. Measured neonicotinoid residues expressed in nectar equivalents (normalized to 0.23 lb c.e./A) in strawberry and grape versus the thiamethoxam colony-level NOAEC and LOAEC toxicity endpoints.

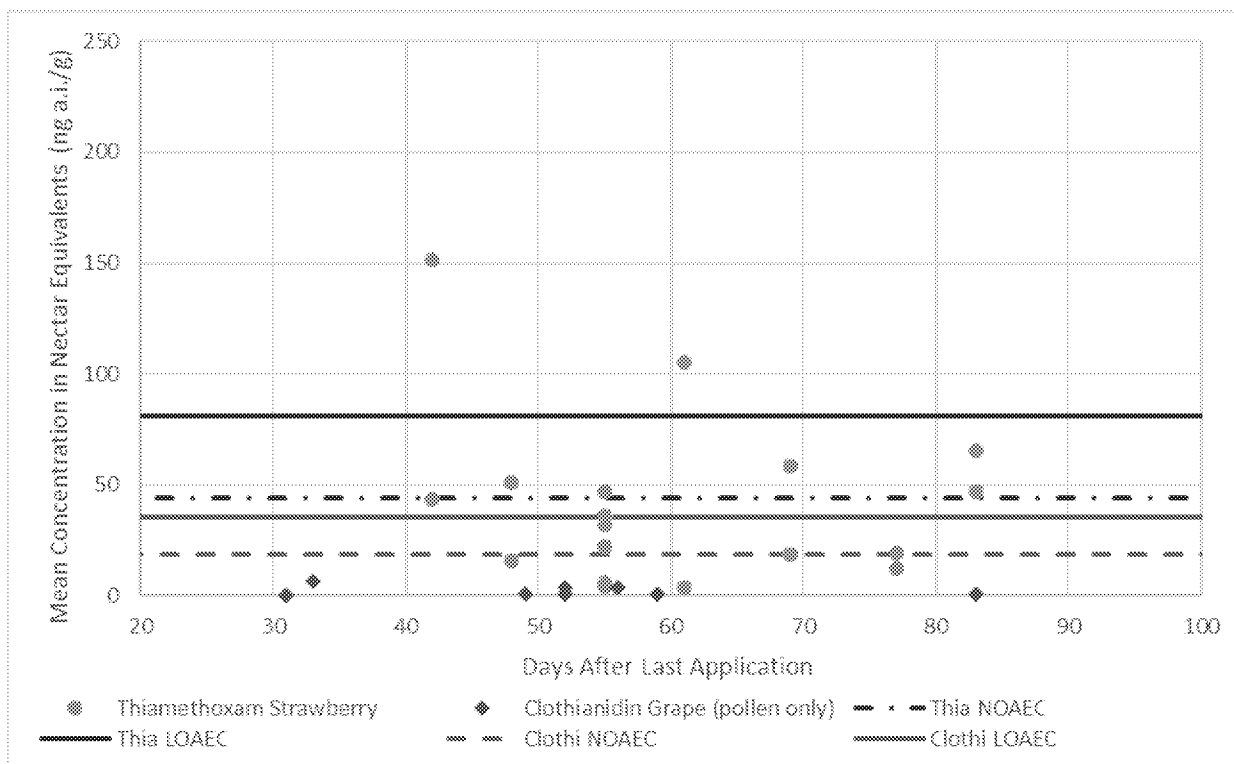


Figure [STYLEREf 1 \s]-24. Measured neonicotinoid residues expressed in nectar equivalents (normalized to 0.16 lb c.e/A) in strawberry and grape versus the thiamethoxam colony-level NOAEC and LOAEC toxicity endpoints.

Thiamethoxam: Soil, post-bloom applications

Only one post-bloom soil application study is available for a neonicotinoid applied to berries (*i.e.*, applications of imidacloprid to blueberries, MRID 49535602). These data are considered here. All blueberry residue data (**Figure 5-25**) are below the colony level endpoints. This suggests low risk to honey bee colonies.

As discussed above, there is some uncertainty in this risk call due to the timing of the samples (*i.e.*, collected 228 d or more before bloom). If post-bloom applications are carried out closer to bloom (of the following year), there is potential that residues will be higher; however, they would need to be at least an order of magnitude greater to pose a risk to colonies.

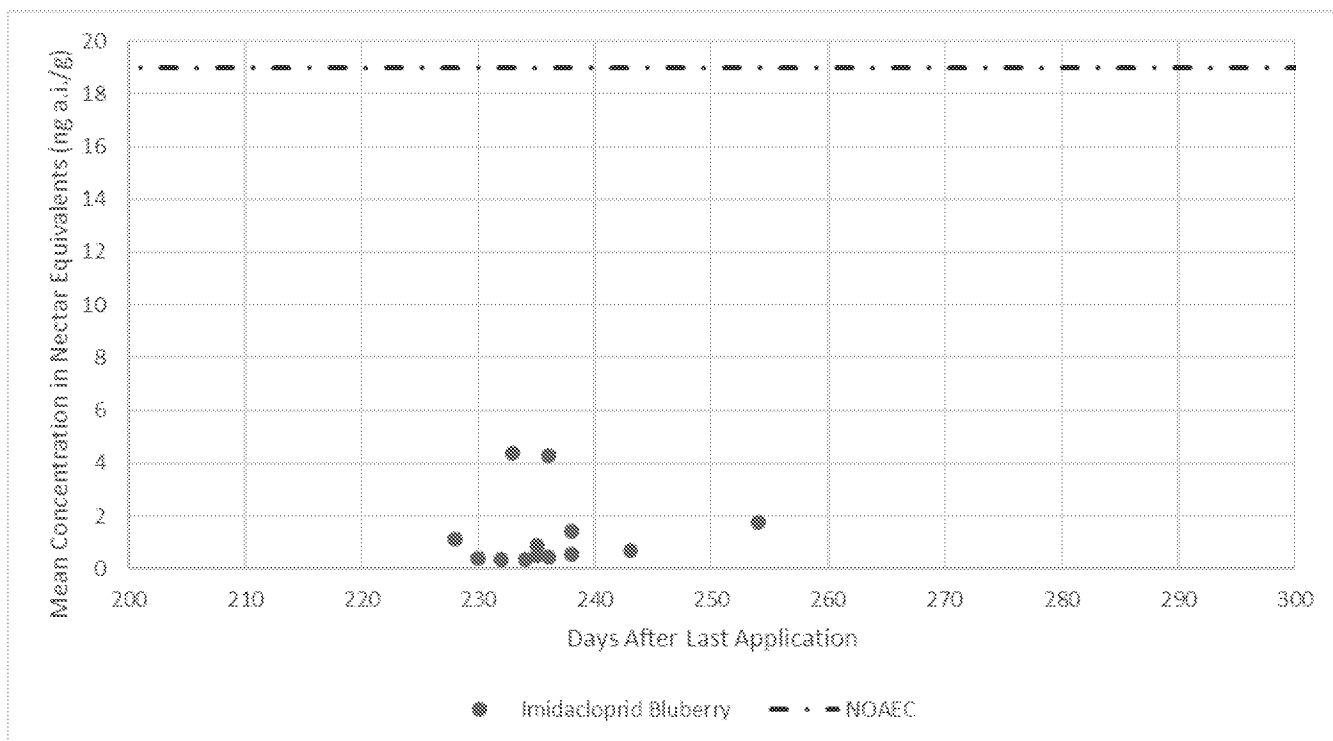


Figure [STYLERE 1 \s]-25. Mean measured residues expressed in nectar equivalents (normalized to 0.23 lb c.e./A) in blueberry from post-bloom soil applications of imidacloprid versus the thiamethoxam colony-level NOAC and LOAC toxicity endpoints.

5.2.2.5 Soybeans

When considering the legume crop group, foliar applications of clothianidin and thiamethoxam are only registered for use on soybeans. Neither chemical is registered for soil applications to soybeans or other legume crops. Clothianidin may be applied twice at a maximum single application rate of 0.1 lb c.e./A. Thiamethoxam may also be applied twice at a maximum single application rate of 0.053 lb c.e./A. When considering the usage data for these two chemicals (provided by BEAD in the SLUA), no information is available for clothianidin. For thiamethoxam, 30,000 lbs are applied per year, representing <2.5% of acres treated (on average or during the maximum single year).

Although bees are not required for pollination of soybeans, the crop is considered attractive to bees. Both nectar and pollen are considered attractive to honey bees (USDA 2017). Consequently, exposure is assessed for honey bees through both pollen and nectar.

This section describes the lines of evidence associated with the assessment of risks of clothianidin and thiamethoxam to honey bee colonies from foliar applications to soybeans. For both chemicals, the lines of evidence suggest that the risk to honey bee colonies is low for this use. This is based on the level of residues being below colony level NOAECs. Additional information is provided in **Table 5-32**.

Table [STYLEREf 1 \s]-32. Lines of evidence considered in risk call for foliar applications of thiamethoxam and clothianidin to soybeans.

Line of evidence		Clothianidin (LOW Risk)	Thiamethoxam (LOW Risk)
Chemical specific residue data		None	Soybean
Residue data for other chemicals		thiamethoxam, imidacloprid	imidacloprid
Percent of clothianidin present in residues		100%	Nectar: 12-97% Anther: 13-54%
Measured data:	Exceedance Attribute	NOAEC/LOAEC	NOAEC/LOAEC (clothi)
	Frequency: Number daily mean residue values > NOAEC & LOAEC	None	None
	Duration: Max Interval (d) since application with NOAEC/LOAEC exceedance	None	none
	Magnitude: Ratio of Max to Clothi NOAEC (% of diet required to reach NOAEC & LOAEC)	0.43x (not calculated)	0.22x (not calculated)
Crop Attractiveness* & Bloom Duration		Nectar and pollen are attractive to honey bees. Bloom duration lasts for 2-3 weeks.	
Managed Pollinators		Not required	
Ecological incidents		None	None
Spatial extent of risk (annual acres treated)		No usage data available	<759,000 (ave) <1,900,000 (max)
Other Considerations		None	

*Based on USDA 2017

Clothianidin

There are no chemical-specific residue data available for clothianidin. Nectar as well as pollen or anther residue data are available for thiamethoxam (MRID 50265503) and imidacloprid (MRIDs 50025901 and 50025902) use as foliar sprays on soybeans. Based on bridging analysis using inter-tissue relationships it was determined that anther data are a reasonable surrogate for residue concentrations in pollen when pollen-specific data are not available. It was also determined that residues could be bridged across neonicotinoid chemicals. A summary of the comparisons of thiamethoxam and imidacloprid residue data as well as the comparisons of pollen and anther residue data is provided in **Attachment 2**.

There were insufficient data to reliably estimate dissipation rate constants for residues in soybean nectar and pollen, therefore, a Monte Carlo analysis was not conducted (to estimate residues over time) for soybean foliar applications.

When normalized to the clothianidin application rate, the available study has measured residues below the clothianidin colony-level NOAEC and LOAEC (**Figure 5-26**). There is uncertainty associated with the

available residue data for soybeans in that it does not include residues for clothianidin. For the two available studies involving thiamethoxam and imidacloprid, comparisons among chemicals was limited because the imidacloprid residue data only included one site. There is uncertainty associated without better understanding the variability of imidacloprid residues (across sites). Average residues would have to be about 10x to exceed the NOAEC for the colony feeding study and 5-15 times higher to exceed the LOAEC. The bridging analysis for foliar neonicotinoid applications (**Attachment 2**) also suggests conservatively characterizing anther residues by applying a 3x factor to estimate a potential upper bound for pollen exposures. Considering the level of residues described in **Figure 5-26**, the use of such a factor with this dataset would result in only a single mean measurement exceeding the clothianidin NOAEC (the maximum mean residue concentration would be 22.9 ng c.e./g for the thiamethoxam Day 5 measurement from Louisiana).

Acknowledging the uncertainties noted above, based on the available data, this analysis concludes that the likelihood of adverse effects to be from the foliar use of clothianidin on soybeans is low.

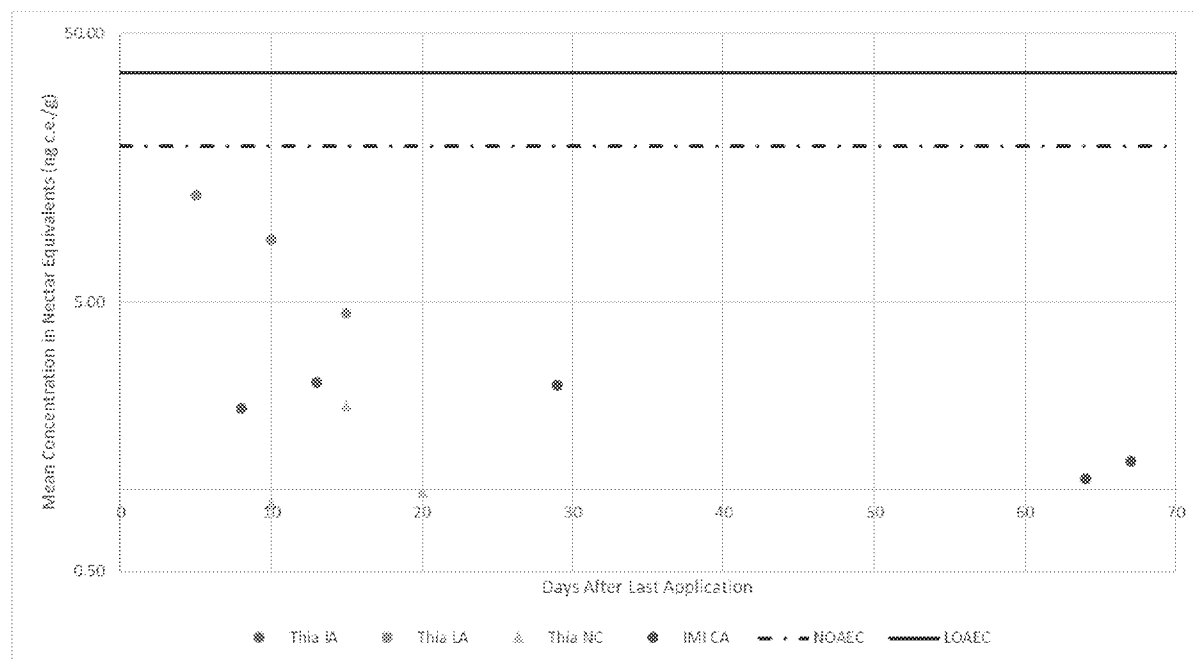


Figure [STYLEREf 1 \s]-26. Measured neonicotinoid residues (normalized to 0.1 lb c.e./A) in soybeans overlaid on colony-level NOAEC and LOAEC.

Thiamethoxam

As discussed above, nectar and anther (surrogate for pollen, as described in the bridging analysis in **Attachment 2**) residue data are available for thiamethoxam foliar applications to soybeans (MRID 50265503). Also available are nectar and pollen residue data for imidacloprid. When normalized to the thiamethoxam application rate, the available study has measured residues below the thiamethoxam colony-level NOAEC and LOAEC (**Figure 5-27**), indicating that the risk to honey bee colonies from foliar applications to soybean is low.

The bridging analysis for foliar neonicotinoid applications (**Attachment 2**) also suggests conservatively characterizing anther residues by applying a 3x factor to estimate a potential upper bound for pollen exposures. Considering the low level of residues described in **Figure 5-27**, using such a factor with this dataset would not change the overall risk conclusion of low risk to honey bee colonies (the maximum mean value would be 12.2 ng c.e./g using this conservative assumption).

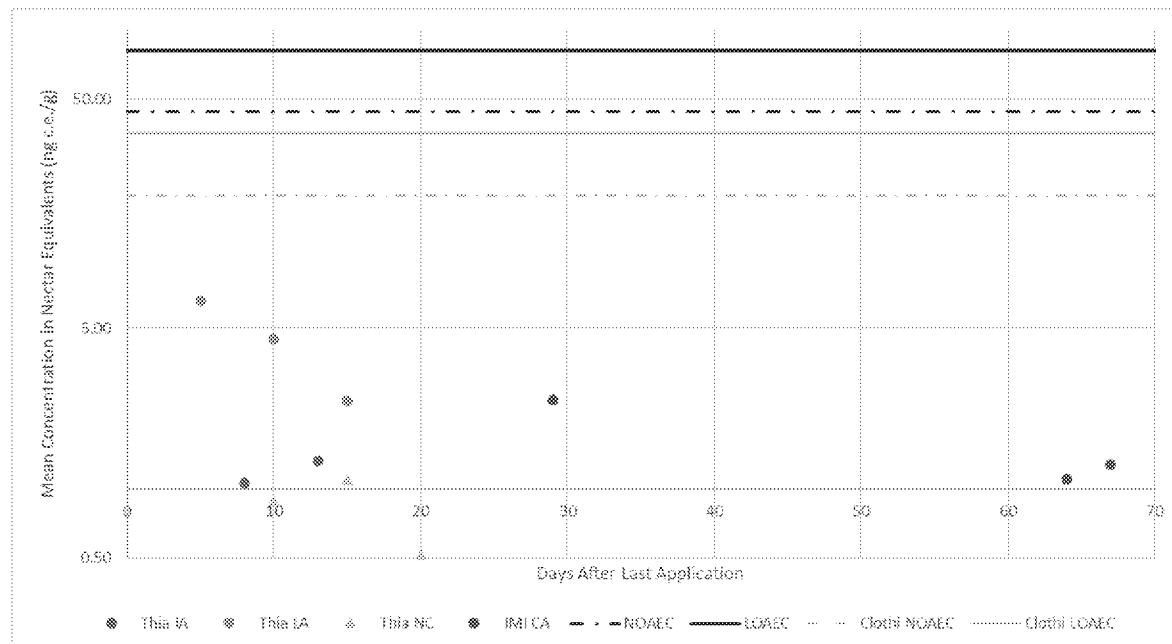


Figure [STYLERE 1 \s]-27. Measured neonicotinoid residues (normalized to 0.053 lb c.e./A) in soybeans overlaid with colony-level NOAEC and LOAEC values.

5.2.2.6 Other Herbaceous Crops

Crops considered below are in some way unique in their respective crop groups (*e.g.*, honeybee attractive where the majority are not, such as chilis), or have no residue data for the crop group (*e.g.*, mint) or are not well represented by the residue data in their respective groups (*e.g.*, potato pollen data are insufficient to represent exposures from sweet potato nectar and pollen). The crops included here include the following honey bee attractive crops:

- Sweet potato, Jerusalem artichoke, edible burdock, dasheen, and horseradish (root and tuber group),
- chillies and peppers³⁰, okra, and roselle (fruiting vegetables group; thiamethoxam only), and
- mint (only registered crop in herbs and species group; thiamethoxam only).

Sweet potatoes have honeybee attractive nectar and pollen while other crops in the root and tuber group are generally either harvested prior to bloom or are not attractive. According to USDA 2017, several root and tuber crops (sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish) produce pollen and/or nectar that is considered attractive to honey bees and other bees. These crops do

³⁰ USDA 2017 includes: Red and cayenne pepper, paprika, chillies (*Capsicum frutescens*; *C. annuum*); allspice, Jamaica pepper (*Pimenta officinalis*)

not require bee pollination or managed pollinators for development of roots and tubers, rather, they are cultivated vegetatively (e.g., through seed pieces or cuttings from roots). One exception is that sweet potatoes need bee pollination when they are bred for seed production. Since these crops may produce flowers during the growing season and their nectar and pollen are honey bee attractive, exposure of bees may occur.

Of the honey bee attractive fruiting vegetables, okra and roselle produce pollen and nectar, while chili peppers only produce pollen. The fruiting vegetables are mainly comprised of crops from the genus *Solanum* (including Eggplant, Tomato), the majority of which do not produce nectar and are not considered attractive to honey bees (USDA 2017). Available pollen residue data for tomato are useful for characterizing exposure to chili peppers; however, they are insufficient for representing the complete exposure from nectar and pollen of okra and roselle. The latter is also the case for available pollen residue data for potatoes being insufficient to represent exposure from sweet potato nectar and pollen. Mint has honeybee attractive pollen and nectar. Given the lack of sufficient nectar and pollen residue data to represent the crops listed above, conclusions from other herbaceous crop groups (including cotton, cucurbits and soybeans) were used for conclusions of these specific crops in the absence of crop specific data (i.e., nectar and pollen producers).

The maximum application rates registered for clothianidin and thiamethoxam are presented below (Table 5-33) for the members of these crop groups. Cotton, cucurbit and soybean application rates are also included and show similar application rates (based on total applied) and suggest conclusions bridged from these groups are applicable. Clothianidin is registered for use on sweet potatoes but not for the herbs and spices crop group (mint) or for fruiting vegetables. There is no usage information available for the crops mentioned above.

Table [STYLeref 1 \s]-33. Application rates for Thiamethoxam and Clothianidin for other herbaceous crops

Chemical	Application Type	Application Rate lb c.e./A x number of apps (total)					
		Sweet Potatos	Okra, Roselle, Chillies and Peppers	Mint	Cotton	Cucurbits	Soybeans
Clothianadin	Foliar	0.05 x 4 (0.2)	NR	NR	0.1 x 2 (0.2)	0.1 x 2 (0.2)	0.1 x 2 (0.2)
	Soil	0.2 x 1 (0.2)	NR	NR	NR	0.2 x 1 (0.2)	NR
Thiamethoxam	Foliar	0.054 x 2 (0.11)	0.07 x 2 (0.14)	0.05 x 3 (0.15)	0.54 x 2 (0.11)	0.075 x 2 (0.15)	0.053 x 2 (0.11)
	Soil	0.16 x 1 (0.16)	0.15 x 1 (0.15)	NR	NR	0.15 x 1 (0.15)	NR

NR – Not Registered

Clothianidin and Thiamethoxam: Risk conclusions for Honey Bee Attractive Crops in the Root and Tuber Group (Sweet potato, Jerusalem artichoke, edible burdock, dasheen, and horseradish)

Risk conclusions are presented here for clothianidin and thiamethoxam use on root and tuber vegetables that are honey bee attractive. Residue data used for estimating tier 2 risks were bridged from cucurbit and oilseed crops. **Table 5-34** summarizes the basis of the risk characterization for these other herbaceous crops. Residue data for potato (*Solanum tuberosum*) pollen and anthers are available, but since potato flowers do not produce nectar, the utility of this information to evaluate root and tuber crops that produce honey bee attractive nectar is limited. Residue loads from potato pollen-only exposures (when adjusted to nectar equivalents) would not exceed colony-level endpoints. Given that there are no nectar residue data in the root and tuber crop group and that the risk conclusions are based on residues from other crop groups, and that there are risk concerns for crops with similar use patterns (e.g., cucurbits and cotton), the available data indicate a potential for effects to honey bee colonies; however, this is considered the weakest evidence of risk.

Table [STYLEREf 1 \s]-34. Lines of evidence considered in risk call for applications of clothianidin and thiamethoxam to root and tuber crops that are honey bee attractive.

Line of evidence	Foliar applications (Weakest evidence of Risk)	Soil Applications (Weakest evidence of Risk)
Chemical specific residue data	NA	NA
Residue data for other chemicals	Bridged from herbaceous crops: cucurbits, soybeans and oilseed	
Basis for risk call	High risk indicated for both cucurbit and oilseed crops	
Bee attractiveness of crops*	Attractive for specific crops: sweet potato	
Managed pollinators*	Not required or no data	
Ecological Incidents	None reported	
Spatial extent of risk (annual acres treated)	No data	

*Based on USDA 2017

For foliar and soil applications, data were bridged from the other herbaceous crop analyses (for those crops that produce pollen and nectar) to draw a conclusion of risk. Specifically, this includes data for cotton (foliar applications), cucurbits (foliar and soil applications) and soybeans (foliar applications). In summary, for foliar applications, available residue data for cotton and cucurbits exceeded CFS endpoints (i.e., there are risk concerns); however, residue data for soybean did not (i.e., risk was considered low). Since it is unknown whether root and tuber crop residues are similar to cotton and cucurbits or to soybeans, there is uncertainty associated with whether foliar applications of clothianidin pose a risk to honey bee colonies. For soil applications, the only comparative residue data available is for cucurbits. For soil applications to cucurbits, residues are above CFS endpoints and therefore there are risk concerns for honey bee colonies. However, given the limits of using disparate crop groups as a surrogate for this crop, this is considered based on a relatively weak weight of evidence. The cotton, cucurbit and soybean sections (above) should be referenced to get an understanding for the basis for the risk conclusion for each group.

As previously noted, there are no usage data to put into perspective the number of acreage affected relative to other crops around the country. According to USDA (2017), sweet potatoes are grown on 113,000 acres in the US; however, sweet potato does not use managed pollinators and only require

pollination for breeding which represents only a small % of that bearing acreage.³¹ Due to the attractiveness and small acreage used for breeding, exposure is possible for foraging honeybees. While the residues and analysis in the sections noted above (cotton and cucurbits) suggest risk on the field scale from foliar applications, the spatial extent of risk (based on total treated acres) is unknown but expected to be small relative to other crops assessed above (due to lower acres grown and used for breeding).

Thiamethoxam: Risk conclusions for Mint

Similar to what was done above for foliar applications to honey bee attractive root and tuber crops, residue data used for assessing colony level risks were bridged from cotton, cucurbits and soybeans (foliar data). **Table 5-35** summarizes the basis of the risk characterization for these crops. Given that there are no nectar and pollen residue data for herbs and spices, and that the risk conclusions mint are based on residues from other crop groups, and that there are risk concerns for crops with similar use patterns (e.g., cucurbits and cotton), the available data indicate a potential for effects to honey bee colonies; however, this is based on the weakest evidence of risk.

Table [STYLEREf 1 \s]-35. Lines of evidence considered in risk call for applications of thiamethoxam to mint.

Line of evidence	Foliar applications (Weakest Evidence of Risk)
Chemical specific residue data	NA
Residue data for other chemicals	Bridged from herbaceous crops: cotton, cucurbits and soybeans
Basis for risk call	risk indicated for both cucurbits and cotton
Bee attractiveness of crops*	Attractive for herbs and spices
Managed pollinators*	Not required or no data
Ecological Incidents	None reported
Spatial extent of risk (annual acres treated)	No data

*Based on USDA 2017

As previously noted, there are no usage data to put into perspective the number of acreage affected relative to other crops around the country. According to USDA (2017), peppermint is grown on about 68,000 acres and does not require bee pollination or use managed pollinators. Additionally, peppermint oil is made from vegetative growth (without flowering or seed production) with no data mentioned on how much is grown for oil versus fresh market. Because these crops are attractive to bees, there is potential exposure from foraging on these crops. While the residues and analysis in the sections noted above (cotton and cucurbits) suggest a risk on the field scale from foliar and soil applications, the spatial extent of risk (based on total treated acres) is unknown but expected to be small relative to other crops assessed above (due to low acres grown and/or acres utilized in breeding or with available attractive flowers). There is the noted uncertainty on what percentage of mint acres are grown for oil production (without flowering or seed production) compared to production that would yield attractive flowers.

³¹ The remaining acres are propagated vegetatively

Thiamethoxam: Risk conclusions for Honey Bee Attractive Fruiting Vegetables (chilies and peppers, okra, and roselle)

Of the fruiting vegetables that are honey bee attractive, okra and roselle produce nectar and pollen while chillis and peppers produce only pollen. Residue data are available for pollen from fruiting vegetables (foliar: tomato, soil: tomato and bell pepper), but not nectar. The proportion of clothianidin residues relative to total residues ranged from 6-95% in pepper pollen (MRID 49804103), 66-88% in tomato flowers (MRID 50023201) and 33-83% in tomato pollen (MRID 50265507) in the soil studies and 5.3-90% in tomato pollen in the foliar study (MRID 49804101). Given the proportion of clothianidin residues in these matrices, both the clothianidin and thiamethoxam colony endpoints are relevant for considering risks to bees.

For chillis and peppers, the available pollen residue data for tomatoes and bell peppers are believed to be an appropriate surrogate because they are in the same crop group (i.e., fruiting vegetables) and same family (i.e., Solanaceae). It should be noted that residue data are available for another species in the Solanaceae family (potato); however, these data are not used for fruiting vegetables because of concern that differences in form (i.e., potatoes produce tubers whereas chillis and peppers do not) may lead to differences in concentrations of neonicotinoids in pollen. **As discussed below, for foliar applications to chillis and peppers, there is the strongest evidence of risk.** This is based on observations of several residues for pollen exceeding the clothianidin and thiamethoxam CFS endpoints. **For soil applications, there is weak evidence of risk for chillis and peppers.**

For okra and roselle, the available pollen residue data for tomatoes and bell peppers are also relevant because they are all in the same crop group. As discussed below, residues in pollen for tomato and chili peppers exceed colony level endpoints, suggesting risk concerns based on pollen alone for both foliar and soil treatments. There is uncertainty in relying only on the tomato and bell pepper pollen data because there are no available residue information for okra or roselle nectar. Also, both of these species are in a different family (i.e., Malvaceae). In order to address these uncertainties, available risk conclusions for foliar applications to cotton, which is also in the Malvaceae family (and which only produces honey bee-attractive nectar), are considered in drawing risk conclusions for okra and roselle. Since application rates for cotton and fruiting vegetables are similar, the risk concerns identified for cotton would also extend to okra and roselle. In extrapolating the honey bee risk conclusions from cotton nectar exposures to okra flowers, only floral nectar was considered (i.e. neither cotton pollen, which was not honey bee attractive or cotton extrafloral nectar, which okra does not produce were considered). When considering soil applications to okra and roselle, residue data for other herbaceous crops are considered. In this case, only cucurbit data are available. Risk concerns were identified as of moderate evidential strength for cucurbits (based on a combination of incident data and residues exceeding the clothianidin CFS NOAEC endpoint, but not any of the thiamethoxam CFS endpoints). As the residue data for soil applications to fruiting vegetables (tomato and pepper) appear fairly similar to the cucurbit data, and for fruiting vegetables no incident data is available to bolster the risk conclusions, the risk concerns for soil applications to okra and roselle are considered fairly weak. **When considering all of the lines of evidence, there is moderate evidence of risk for foliar applications to okra and roselle and weakest evidence of risk for soil applications to okra and roselle,** based on the uncertainties associated with extrapolating from other herbaceous crops. Risk conclusions are presented below **Table 5-36** for thiamethoxam use on honey bee attractive fruiting vegetable crops.

Table [STYLEREf 1 \s]-36. Risk conclusions for okra, roselle, chillies and peppers for thiamethoxam.

Line of evidence	Foliar applications (Strongest Evidence of Risk for Chilis and Peppers, Moderate Evidence of Risk for Okra and Roselle)	Soil Applications (Moderate Evidence of Risk for all crops)
Chemical specific residue data*	Tomato	Chili pepper, tomato
Crop-specific residue data for other chemicals	Tomato (dinotefuran)	Bell pepper (dinotefuran) Tomato (dinotefuran and imidacloprid)
Basis for risk call	Colony level exceedances for pollen only residues from both foliar (bridged) and soil (chemical specific and bridged) data	
Bee attractiveness of crops**	Attractive for specific crops: Red and cayenne pepper, paprika, chilies (Capsicum frutescens; C. annuum); allspice, Jamaica pepper (Pimenta officinalis), okra, roselle	
Managed pollinators required**	No	
Incidents	None reported	
Spatial extent of risk (annual acres treated)	No data	
Other considerations	Residue data are not available for nectar, which is a limitation for okra and roselle. This is not a limitation for chilis and peppers, which only produce pollen.	

*Residue data are only available for pollen.

**Based on USDA 2017

Foliar applications

For foliar applications tomato pollen residue data available for thiamethoxam and dinotefuran are used to evaluate potential exposures to honey bee colonies from okra, roselle, chilis and peppers. Exposure to colonies based on pollen exposure alone is presented below in **Figure 5-28**. It is assumed that these data (for tomatoes MRIDs 4980401 (thiamethoxam) and 49841004 (dinotefuran)) are representative of residues from other fruiting vegetables. Note that the pollen residues are adjusted to nectar equivalents to compare them to the clothianidin and thiamethoxam colony level endpoints. Considering the thiamethoxam-specific data for foliar application to tomatoes, measured residue concentrations exceed both the colony-level NOAEC and LOAEC up to about 10 days after last application of thiamethoxam.

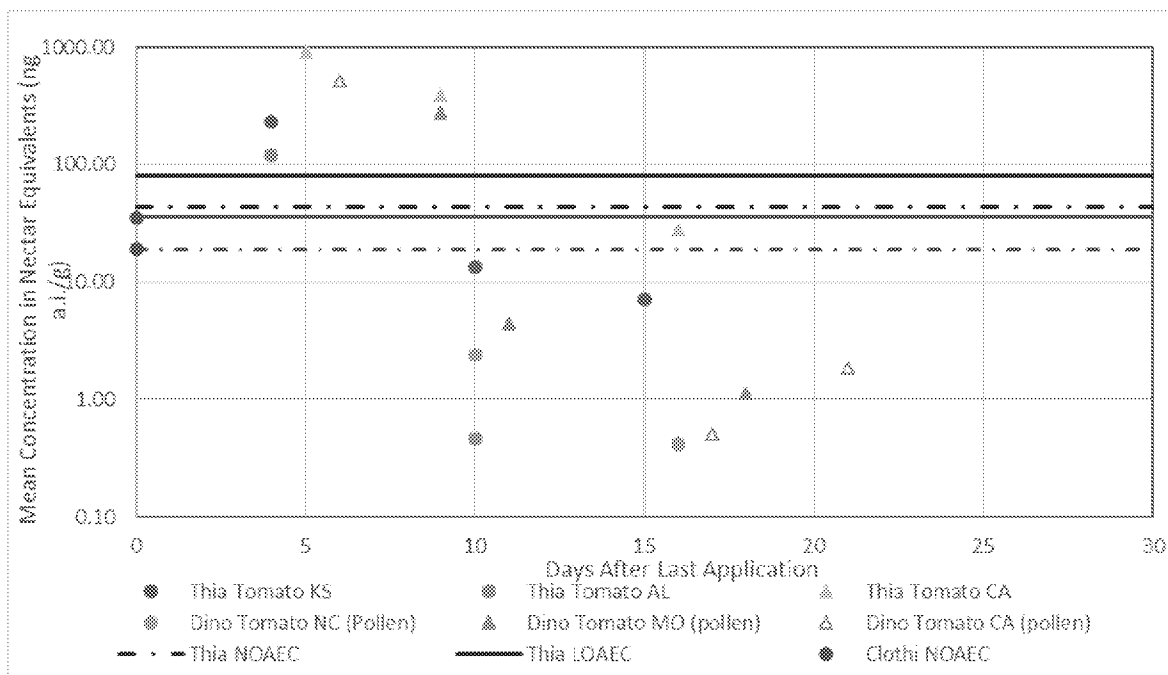


Figure [STYLERE 1 \s]-28. Measured thiamethoxam and dinotefuran residues (normalized to 0.07 lb c.e./A the thiamethoxam foliar application rate) in tomatoes (pollen only) overlaid on colony-level NOAEC and LOAEC values.

Soil applications

For soil applications, chemical-specific, pollen residue data are available for thiamethoxam (chili pepper – MRID 49804103 and tomato – MRID 50265507). Data are also available for dinotefuran (tomato – MRID 49841004 and bell pepper – MRID 50145702) as well as imidacloprid (tomato – MRID 49665201). Since the bridging analysis concluded that residues could be bridged across chemicals and crops, all the available data are used to represent potential exposures to honey bee colonies from thiamethoxam applications to okra, roselle, chilis and peppers. Exposures to colonies, based on pollen exposure alone are presented below in **Figure 5-29**. Pollen residues depicted in this figure are adjusted to nectar equivalents to allow comparison with colony level endpoints.

As discussed previously, the total residue of concern for thiamethoxam is represented by both thiamethoxam and clothianidin (as a degradate). When considering the relative proportion of the two chemicals in the total residue of fruiting vegetable pollen (that received soil treatments), the two residues were approximately the same proportion. Therefore, the endpoints for both clothianidin and thiamethoxam colony studies are considered in evaluating potential colony level risk.

Considering the thiamethoxam-specific data for soil application to chili peppers, residue concentrations do not no exceed the colony-level NOAEC and LOAEC values. There is a single data point for dinotefuran concentrations in tomato that is above the thiamethoxam colony level endpoints as well as clothianidin. Consequently, when considering the whole data set for pollen producing crops in the fruiting vegetable crop group, there are exceedances of the colony level NOAEC and LOAEC values for both residues of concern, suggesting a potential for colony level risk. Because only a few of the data points exceed the colony level endpoints, and only a single data point exceeds the thiamethoxam endpoints, these data

represent weak evidence of risk. In addition, there is uncertainty for okra and roselle risk conclusions due to a lack of exposure information for nectar.

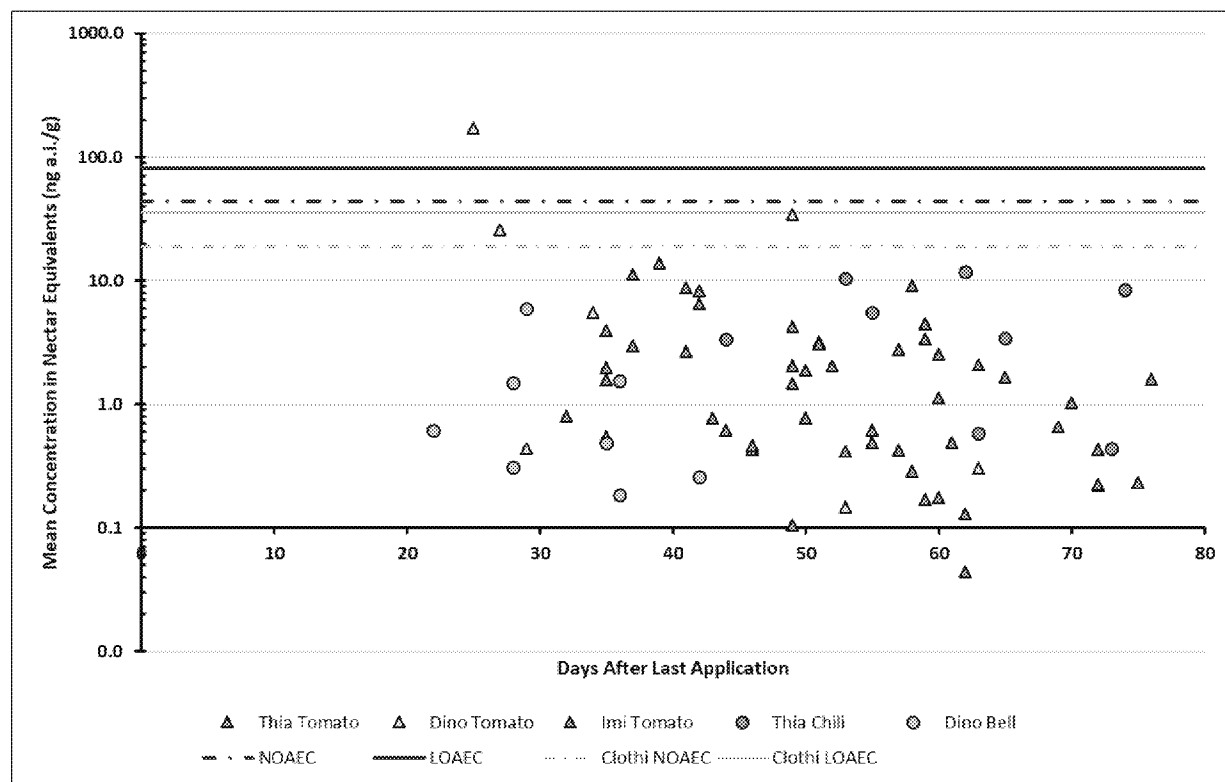


Figure [STYLEREf 1 \s]-29. Figure Y. Measured thiamethoxam and dinotefuran residue concentrations (normalized to 0.15 lb c.e./A the thiamethoxam soil application rate) in fruiting vegetables producing pollen only overlaid with the colony-level NOAEC and LOAEC.

While chili peppers do not use managed honeybees for pollination they do require bee pollination. As with other members of this crop group, the spatial extent of risk is uncertain due to a lack of information on usage for chili peppers. According to USDA 2017, there are 71,000 US bearing acres of peppers. While chili peppers are attractive pollen producers and residue data suggest the potential for colony level risk, the document does not delineate between chili and bell peppers in the 71,000 acres. Additionally, USDA 2017 notes that the chili and pepper group may be grown in glasshouses, with bumble bees for pollination which could limit honeybee exposure as well.

5.2.2.7 Non-Agricultural Uses

The non-agricultural crop group encompasses a wide variety of uses; for the purposes of this assessment only those uses which present a complete exposure pathway for honeybees are included. These crops include ornamentals, residential turf, and forestry and non-bearing fruit and nut trees (the latter registered for clothianidin use only). Clothianidin and thiamethoxam are registered for applications to a diverse group of ornamental species. For foliar and liquid soil applications to both ornamental plants and turf, the maximum single and seasonal application rate is 0.41 lb ai/A for clothianidin and 0.266 lb ai/A for thiamethoxam (normalized to clothianidin equivalents).

Usage data for clothianidin and thiamethoxam on these non-agricultural use sites were not available from the Screening Level Usage Analysis (SLUA). The attractiveness of ornamentals and turf crops vary widely, however some members in each group are considered to be attractive to bees. Consequently, there is the potential for exposure for bees on treated sites.

5.2.2.7.1 Ornamental Plants

Clothianidin and thiamethoxam are registered for applications to a diverse group of ornamental species, including non-bearing fruit and nut trees, using a variety of methods including foliar spray, broadcast granular, soil drench, soil injection, and basal bark applications in nurseries (grassy areas, field nurseries or containerized ornamentals), commercial properties and residential properties. For foliar and soil applications, the maximum single and seasonal application rate is 0.41 lb ai/A for clothianidin and 0.266 lb ai/A (in clothianidin equivalents) for thiamethoxam. Given the wide variety of species included in this group, including many cultivated specifically to produce large attractive blooms and including ornamental versions of species known to produce honey bee-attractive floral matrices (*e.g.* cherry trees), this use site is assumed to produce honey bee attractive pollen and nectar.

This section describes the lines of evidence associated with the assessment of risks of clothianidin and thiamethoxam to honey bee colonies from foliar and soil applications to ornamental plants. **Overall, there is strong evidence indicating that use of clothianidin and thiamethoxam on attractive ornamental plants pose risks to honey bee colonies foraging on treated sites.** The lines of evidence supporting this conclusion include high thiamethoxam residues in multiple tested ornamental species, requiring that colonies consume a relatively small (3.9-43.5%, see **Tables 5-37** and **5-38** below) proportion of their diet to reach sufficient concentrations to exceed exposures observed to result in colony level effects. Further, these residue levels exceed the colony level NOAEC and/or LOAEC endpoints past the last days that samples were taken (~3 weeks following application). Although clothianidin-specific residue data are not available, the overall analysis presented in the neonicotinoid foliar and soil application bridging strategy document (**Attachment 2**) suggest that chemical influence on the level of residues in a given crop is generally limited when residues are normalized by application rate and date. Although the residue data described in this section is limited to herbaceous plants, the risk conclusions for orchard crops described in the previous agricultural crop section provide support that risk conclusions would be similar between herbaceous and woody ornamental plants. Further, the risk conclusions presented here are additionally supported by three available beekill incident reports following soil applications of clothianidin to either urban or residential trees. Two of the incidents were determined to be registered uses while the legality of the use was undetermined in the third. In two of the incidents, the attribution of the incident to the use of clothianidin was determined to be possible, while it was probable in the third. In all three incidents, the use of imidacloprid may also have contributed to the incident (two of the incidents occurred after the use of Bayer Advanced, a granular soil application containing both clothianidin and imidacloprid, and both imidacloprid and clothianidin residues were also detected in dead bee samples from the third incident).

As described in detail below, data for thiamethoxam are available to characterize exposure to honeybees from ornamental uses. The method for evaluating these data are summarized in **Attachment 3**. There are general uncertainties with data on ornamental uses. Many application rates do not readily scale to a per acre use for standard evaluation and usage data for ornamentals are not readily available. The figures summarize residue data based on nectar only. Pollen from the ornamental dataset, when adjusted to total nectar equivalents, would generally contribute only about 2% of the

overall total nectar equivalent residue expression, so it was considered to have negligible impact on risk conclusions.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]7. Lines of evidence considered in risk call for foliar and soil applications of clothianidin to ornamental plants

Line of evidence		Clothianidin, Foliar (Strongest Evidence of Risk)		Clothianidin, Soil (Strongest Evidence of Risk)	
Chemical specific residue data		No data		No data	
Residue data for other chemicals		Thiamethoxam (stargazer lily, mock orange, lilac)		Thiamethoxam (lilac, hedge cotoneaster, Sargeant crabapple, stargazer lilly)	
Exposure	Exceedance Attribute	NOAEC (19 µg ce/g)	LOAEC (35.6 µg ce/g)	NOAEC (19 µg ce/g)	LOAEC (35.6 µg ce/g)
Measured Data (all neonics)	Frequency: Number daily mean residue values > NOAEC & LOAEC	18	18	12	8
	Duration: Number of days > NOAEC & LOAEC	21	21	23	23
	Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	47.3x (2.1%)	25.3 (3.9%)	15.1 (6.6%)	8.1 (12.4%)
Measured data (clothianidin)	Frequency: Number daily mean residue values > NOAEC & LOAEC	N/A	N/A	N/A	N/A
	Duration: Number of days > NOAEC & LOAEC	N/A	N/A	N/A	N/A
	Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	N/A	N/A	N/A	N/A
Crop Attractiveness* & Bloom Duration		Highly attractive (nectar and pollen); long bloom duration			
Managed Pollinators		Generally not			
Ecological incident reports		None		One incident reported for a bumble bee kill following use on linden trees in an urban center. Clothianidin was detected in bee and plant tissues (concentrations not reported). Two other residential (home-owner) incidents occurred where honey bees died following soil applications to residential trees (no samples taken).	
Spatial extent of risk (annual acres treated)		No usage information available			

Line of evidence	Clothianidin, Foliar (Strongest Evidence of Risk)	Clothianidin, Soil (Strongest Evidence of Risk)
Other considerations	Residues, based on nectar exposure alone, exceed the CFS endpoints for multiple species and locations	Residues, based on nectar exposure alone, exceed the CFS endpoints for multiple species and locations

*Assumed based on diverse variety of species and the nature of the use site (desired showy blooms for many ornamental species)

¹ Maximum measured mean value was for samples taken 7 days and 23 after last application for foliar and soil applications, respectively.

Table [STYLEREf 1 \s]-38. Lines of evidence considered in risk call for foliar and soil applications of thiamethoxam to ornamental plants.

Line of evidence		Thiamethoxam, Foliar (Strongest Evidence of Risk)				Thiamethoxam, Soil (Strongest Evidence of Risk)			
Chemical specific residue data		stargazer lily, mock orange, lilac				lilac, hedge cotoneaster, crabapple, stargazer lily			
Residue data for other chemicals		No data				No Data			
Percent of clothianidin present in residues (average)		Median: 21%; Mean: 26%; Range: 4-66%				Median: 30%; Mean: 38%; Range: 1-98%			
Exposure	Exceedance Attribute	Clothi NOAEC	Clothi LOAEC	Thia NOAEC	Thia LOAEC	Clothi NOAEC	Clothi LOAEC	Thia NOAEC	Thia LOAEC
Measured Data (all neonics)	Frequency: Number daily mean residue values > NOAEC & LOAEC	18	15	13	7	8	8	6	4
	Duration: Number of days > NOAEC & LOAEC	21	21	21	10	23	23	23	23
	Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	30.7x (3.3%)	16.4x (6.1%)	13.3x (7.5%)	7.2x (13.9%)	9.8 (10.2%)	5.2 (19.1%)	4.2 (23.6%)	2.3 (43.5%)
Measured data (thiamethoxam)	Frequency: Number daily mean residue	18	15	13	7	8	8	7	4

Line of evidence		Thiamethoxam, Foliar (Strongest Evidence of Risk)				Thiamethoxam, Soil (Strongest Evidence of Risk)			
	values > NOAEC & LOAEC								
	Duration: Number of days > NOAEC & LOAEC	21	21	21	10	23	23	23	23
	Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC)	30.7x (3.3%)	16.4x (6.1%)	13.3x (7.5%)	7.2x (13.9%)	9.8 (10.2%)	5.2 (19.1%)	4.2 (23.6%)	2.3 (43.5%)
Crop Attractiveness* & Bloom Duration		Highly attractive (nectar and pollen); long bloom duration (Indeterminate bloom)							
Managed Pollinators		Generally not							
Tier II or III Data		None							
Ecological incident reports		None							
Spatial extent of risk (annual acres treated)									
Other considerations		Residues, based on nectar exposure alone, exceed the thiamethoxam CFS endpoints for multiple species and locations				Residues, based on nectar exposure alone, exceed the thiamethoxam CFS endpoints for multiple species. Only residues from a single site (NY) exceed the thiamethoxam CFS endpoints.			

*Assumed based on diverse variety of species and the nature of the use site (desired showy blooms for many ornamental species)

¹ Maximum measured mean value was for samples taken 7 days or 23 days after last application for foliar and soil applications, respectively.

Clothianidin: Foliar applications

Registrant submitted studies are not available to estimate the residues in ornamental plants after foliar applications of clothianidin. Although clothianidin-specific residue data are not available, the overall analysis presented in the neonicotinoid foliar and soil application bridging strategy document (**Attachment 2**) and demonstrated as well in the previous agricultural crop sections in this risk assessment, suggest that chemical influence on the level of residues in a given crop is relatively low when residues are normalized by application rate and timing. Therefore, thiamethoxam ornamental data were used as a surrogate for potential clothianidin exposures.

[REF_Ref524041487 \h * MERGEFORMAT]5-30 below shows neonicotinoid residues in ornamentals following foliar applications are greater than the colony level NOAEC up to at least 21 days when normalized to the maximum clothianidin seasonal application rate of 0.41 lb ai/A. Mean-measured residues (normalized to total application rate) from foliar applications of thiamethoxam to ornamental plants range from 6.29 to 1227.43 ng c.e./g. with 18 values (86%) over both the clothianidin CFS NOAEC and LOAEC endpoints. At the maximum mean-measured application-normalized concentration of 1227 ng c.e./g, honey bee colonies would need to consume only 2.1% of their diet to reach the NOAEC (3.9% to reach the LOAEC), suggesting that the availability of alternative sources of forage may be unlikely to change the risk conclusions. Additionally, all three tested ornamental species had residues exceeding the colony level LOAEC and the only residues below the LOAEC were for stargazer lily samples collected from Wisconsin, while all the lily samples from the other two sites (Oregon and New York) were above the LOAEC. Finally, the figure below shows data based on exposure to nectar only. Pollen would generally contribute only about 2% of the residue expression, so it was considered to have negligible impact on residue concentrations. This data suggests that residues from foliar applications to ornamental plants may be high enough to pose risk to foraging honey bees.

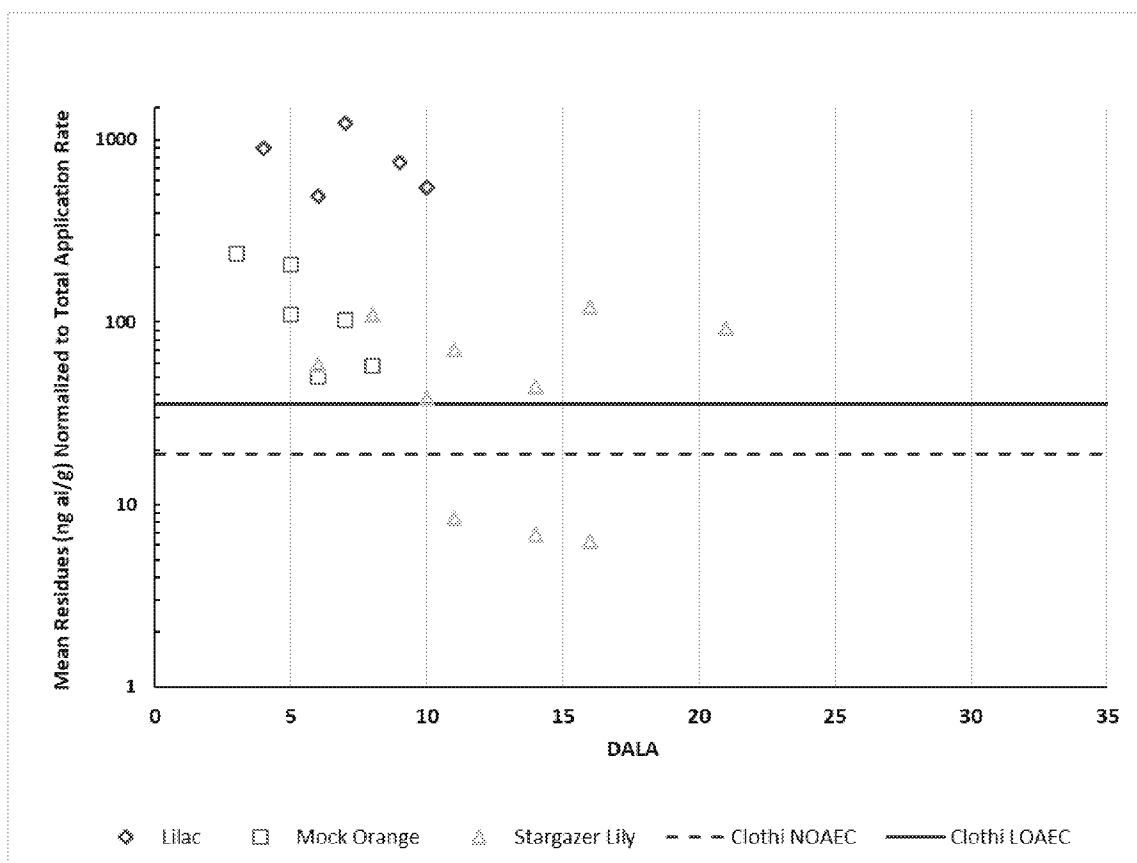


Figure [STYLERE 1 \s]-30. Measured thiamethoxam residue data in nectar (normalized to 0.41 lb c.e./A total application) versus the clothianidin CFS NOAEC and LOAEC endpoints (19 and 35.6 ng c.e./g, respectively) for the ornamental plant group.

Clothianidin: Soil applications

Registrant submitted studies are not available to estimate the residues in ornamental plants after soil applications of clothianidin. Although clothianidin-specific residue data are not available, the overall analysis presented in the neonicotinoid foliar and soil application bridging strategy document (**Attachment 2**) and demonstrated as well in the previous agricultural crop sections in this risk assessment, suggest that chemical influence on the level of residues in a given crop is relatively low when residues are normalized by application rate and timing. Therefore, thiamethoxam ornamental data were used as a surrogate for potential clothianidin exposures. Limited additional residue data is also available for imidacloprid and dinotefuran soil applications from registrant-submitted and open literature data. However, these data used application rates that were difficult to compare to clothianidin applications and were thus excluded from the current analysis. Additionally, the risk conclusions described below, based on the available thiamethoxam data, were determined to be unlikely to be impacted by consideration of this other data. For more information, see the concurrently published imidacloprid and dinotefuran bee risk assessments (USEPA, 2019x-y).

[REF_Ref524041487 \h * MERGEFORMAT]5-31 below shows neonicotinoid residues in ornamentals following soil applications are greater than the colony level NOAEC up to at least 23 days when normalized to the maximum clothianidin seasonal application rate of 0.41 lb ai/A. Mean-measured residues (normalized to total application rate) from soil applications of thiamethoxam to ornamental

plants range from <0.5 to 287 ng c.e./g. with 12 and 8 values over both the clothianidin CFS NOAEC and LOAEC endpoints. At the maximum mean-measured application-normalized concentration of 287 ng c.e./g, honey bee colonies would need to consume only 6.6% of their diet to reach the NOAEC (12.4% to reach the LOAEC), suggesting that the availability of alternative sources of forage may be unlikely to change the risk conclusions. Additionally, all four tested ornamental species had residues exceeding the colony level NOAEC with three of the four species having residues exceeding the colony level LOAEC. Other than one sample, the Sargent crabapple data were all below the colony level NOAEC. However, this data is considered the most uncertain of this dataset as these samples were for whole flowers and were converted to nectar residue values using a conversion factor of 0.25x (as suggested by the residue bridging strategy in **Attachment 2** when nectar data is not collected). The residue bridging strategy also suggests further characterizing whole flower data qualitatively, by using it as a 1:1 surrogate for nectar as an upper bound estimate. Using this conservative extrapolation would add further weight to an overall conclusion of honey bee risk posed by soil applications of clothianidin as it would shift approximately 1/3 of the Sargent crabapple residues above the CFS NOAEC. The tested site locations for these plants were in Oregon, New York, and Wisconsin and it is notable that only residues in nectar samples from the New York sites were above the colony level endpoints, although for lilacs, nectar data were only available for New York. Although lilac nectar data were only available for New York, whole flower lilac data are available for the other sites and were considered (**Figure 5-31**). After converting the lilac flower data to nectar equivalents using the 0.25x conversion factor, an exceedance of the colony level endpoints was also observed for the Wisconsin site (54 ppb on day 13), in addition to the New York site. Finally, the figure below shows data based on exposure to nectar only. Pollen in these species would generally contribute only about 2% of the residue expression (**Attachment 3**), so it was considered to have negligible impact on residue concentrations. Overall, this data suggests that residues from soil applications of clothianidin to ornamental plants may be high enough to pose risk to foraging honey bees.

In addition, three incidents have been reported to the Agency, following soil applications of clothianidin to either urban or residential trees. Two of the incidents were determined to be registered uses while the legality of the use was undetermined in the third. In two of the incidents, the attribution of the incident to the use of clothianidin was determined to be possible, while it was probable in the third. In all three incidents, the use of imidacloprid may also have contributed to the incident (two of the incidents occurred after the use of Bayer Advanced, a granular soil application containing both clothianidin and imidacloprid, and both imidacloprid and clothianidin residues were also detected in dead bee samples from the third incident).

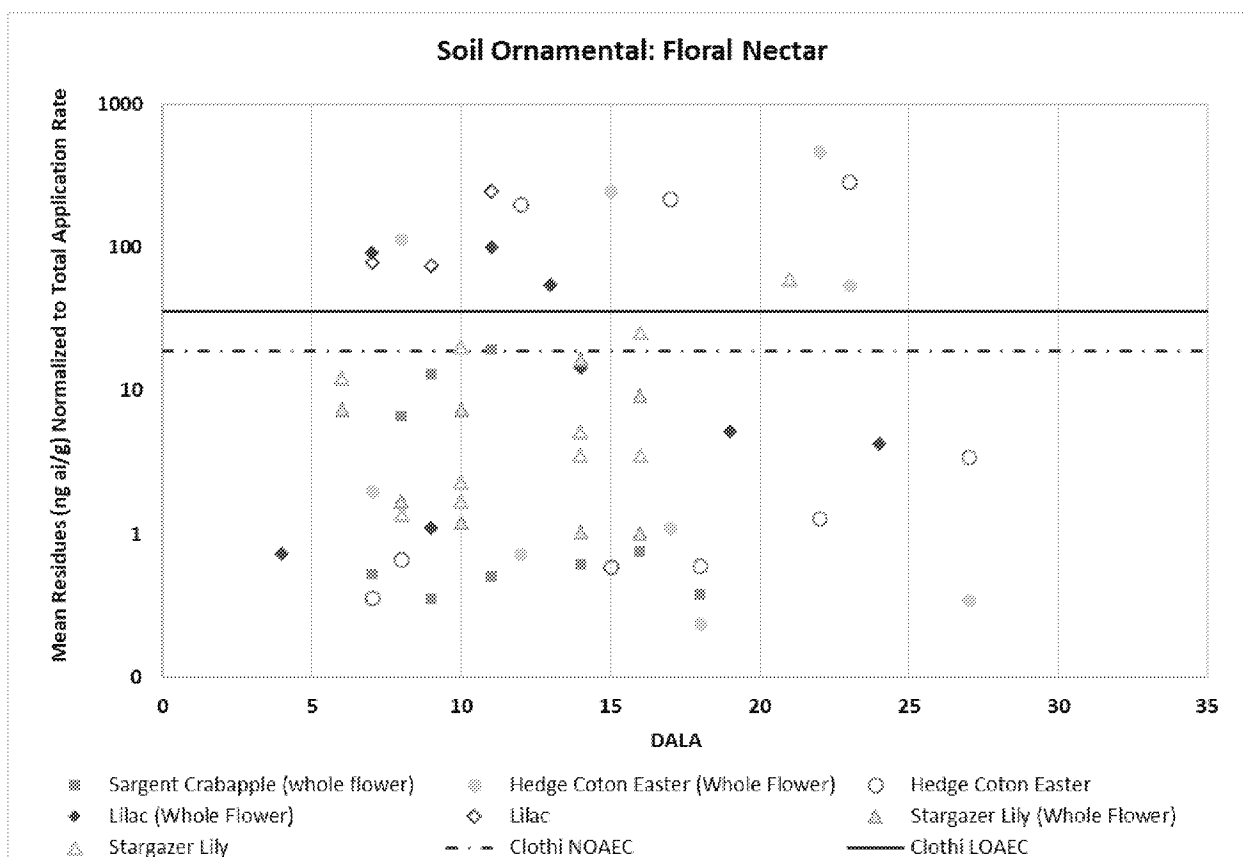


Figure [STYLERE 1 \s]-[SEQ Figure * ARABIC \s 1]1. Measured thiamethoxam residue data (normalized to 0.41 lb c.e./A total application) in nectar (open symbols) and whole flower (solid symbols) versus the clothianidin CFS NOAEC and LOAEC endpoints (19 and 35.6 ng c.e./g, respectively) for the ornamental plant group. Residues in whole flowers were converted to nectar equivalents by applying a conversion factor of 0.25x to the whole flower residue samples.

Thiamethoxam: Foliar applications

There is one study (MRID 504425903) that evaluates thiamethoxam residues following foliar applications to ornamental species including lilac, mock orange, and stargazer lily grown in Oregon, New York and Wisconsin. The study used two foliar applications at a 0.133 lb c.e./A application rate each with a seven day retreatment interval (total rate of 0.266 lb c.e./A).

[REF_Ref524041487 \h * MERGEFORMAT]5-32 below shows thiamethoxam residues in ornamentals following foliar applications are greater than the colony level NOAEC up to at least 21 days when normalized to the maximum thiamethoxam seasonal application rate of 0.266 lb ai/A. Mean-measured residues (normalized to total application rate) from foliar applications of thiamethoxam to ornamental plants range from 4.1 to 796.3 ng c.e./g, with 13 and 7 values over the thiamethoxam CFS NOAEC and LOAEC endpoints. The highest residues were for lilac while residues in mock orange and stargazer lily are more variable and lower. At the maximum mean-measured application-normalized concentration of 796 ng c.e./g, honey bee colonies would need to consume only 7.5% of their diet to reach the thiamethoxam CFS NOAEC (13.9% to reach the LOAEC), suggesting that the availability of alternative sources of forage may be unlikely to change the risk conclusions. Further, compared to the clothianidin

CFS endpoints, honey bee colonies would need to consume only 3.3% and 6.1% of their diet to exceed the clothianidin NOAEC and LOAEC, respectively. Additionally, all three tested ornamental species had residues exceeding the thiamethoxam colony level LOAEC and the only residues below the thiamethoxam NOAEC were for stargazer lily samples collected from Wisconsin, while residues in plants grown in the New York and Oregon sites were higher. Finally, the figure below shows data based on exposure to nectar only. Pollen would generally contribute only about 2% of the residue expression, so it was considered to have negligible impact on residue concentrations. This data suggests that residues from foliar applications to ornamental plants may be high enough to pose risk to foraging honey bees.

As discussed previously, the total residues of concern of thiamethoxam are composed of both thiamethoxam and clothianidin. In the available thiamethoxam foliar studies with ornamentals, both chemicals were found in nectar. In nectar, clothianidin represented 26% of the total residue (on average; range: 4-66%), though it tended to represent more of the total expression in stargazer lily (mean 24%) and mock orange (mean 41%) than in lilac (mean of only 7%). This indicates that both the thiamethoxam and clothianidin CFS endpoints should be considered in evaluating the risk to ornamentals. Since residues exceed both the clothianidin and thiamethoxam CFS NOAEC and LOAEC values, the conclusion that this use poses a risk to honey bee colonies is not influenced greatly by the proportion of thiamethoxam and clothianidin in the total residues.

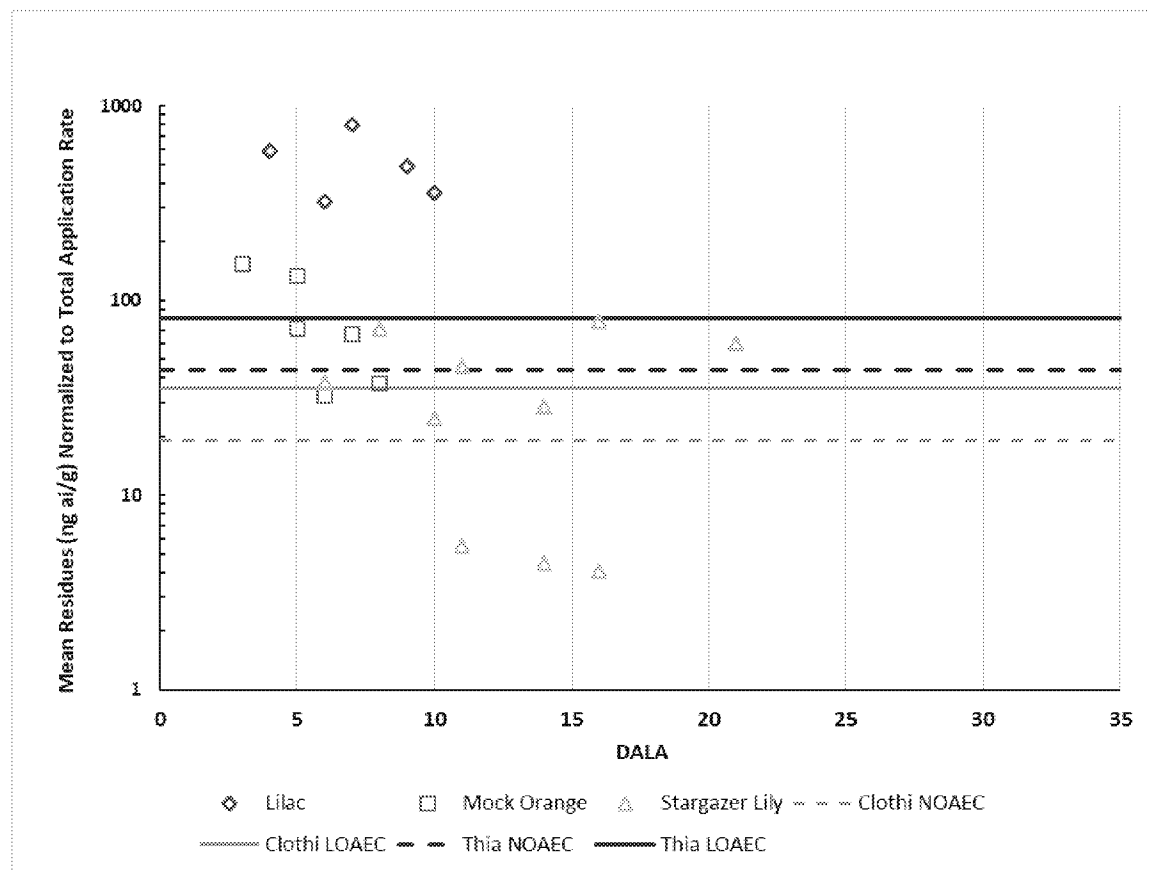


Figure [STYLEREf 1 \s]-32. Mean concentrations of thiamethoxam (in clothianidin equivalents adjusted to the maximum seasonal foliar rate of 0.266 lb a.i./A) in ornamental plant nectar following foliar application. Thicker red dashed and solid horizontal lines represent the thiamethoxam honey

bee colony-level NOAEC and LOAEC (44 and 81 ng c.e./g, respectively). Thinner blue dashed and solid horizontal lines represent the clothianidin NOAEC and LOAEC endpoints (19 and 35.5 ng c.e./g, respectively) for comparison.

Thiamethoxam: Soil Applications

There is one study (MRID 504425903) that evaluates thiamethoxam residues following soil applications to ornamental species including lilac, hedge cotoneaster, stargazer lily and Sargent crabapple grown in Oregon, New York and Wisconsin. The study used two soil applications at approximately a 0.133 lb c.e./A application rate each with a seven-day retreatment interval (total application rate of 0.266 lb c.e./A). Nectar residues were evaluated in each crop, except for the Sargent crabapple, where whole flower samples were taken.

[REF_Ref524041487 \h * MERGEFORMAT]5-33 below shows thiamethoxam residues in ornamentals following soil applications are greater than both the thiamethoxam colony level NOAEC and LOAEC up to at least 23 days when normalized to the maximum thiamethoxam seasonal application rate of 0.266 lb ai/A. For nectar samples, mean-measured residues (normalized to total application rate) from soil applications of thiamethoxam to ornamental plants range from <1 to 186 ng c.e./g, with 6 and 4 values over the thiamethoxam CFS NOAEC and LOAEC endpoints. The highest residues were for lilac and hedge cotoneaster while residues in stargazer lily and Sargent crabapple were lower and did not exceed the thiamethoxam colony level endpoints. At the maximum mean-measured application-normalized concentration of 186 ng c.e./g, honey bee colonies would need to consume only 23.6% of their diet to reach the thiamethoxam CFS NOAEC (43.5% to reach the LOAEC), suggesting that the availability of alternative sources of forage may be unlikely to change the risk conclusions. Further, compared to the clothianidin CFS endpoints, honey bee colonies would need to consume only 10.2% and 19.1% of their diet to exceed the clothianidin NOAEC and LOAEC, respectively. Two of the four tested ornamental species (hedge cotton easter and stargazer lily) had residues exceeding the thiamethoxam colony level LOAEC. The tested site locations for these plants were in Oregon, New York, and Wisconsin and it is notable that for all the nectar data, only residues in samples from the New York sites were above the colony level endpoints (although lilac nectar data was also only available for New York). Although lilac nectar data were only available for New York, whole flower lilac data are available for the other sites and (after converting the lilac flower data to nectar equivalents using the 0.25x conversion factor suggested in **Attachment 2**), there were still no other sites with an exceedance of the thiamethoxam CFS endpoints, although one mean sample from Wisconsin (35.4 ppb on day 13) would approach the clothianidin LOAEC endpoint.

As discussed previously, the total residues of concern of thiamethoxam are composed of both thiamethoxam and clothianidin. In the available thiamethoxam soil studies with ornamentals, both chemicals were found in nectar. In nectar, clothianidin represented 38% of the total residue (on average; range: 13-98%), though it tended to represent more of the total expression in stargazer lily (mean 60%) than in hedge cotoneaster (mean 34%) and lilac (mean 41%). Sargent crabapple had similar contributions of clothianidin relative to thiamethoxam in whole flower samples, with an average of 48% clothianidin contribution. This indicates that both the thiamethoxam and clothianidin CFS endpoints should be considered in evaluating the risk to ornamentals. Since residues exceed both the clothianidin and thiamethoxam CFS NOAEC and LOAEC values, the conclusion that this use poses a risk to honey bee colonies is not influenced greatly by the proportion of thiamethoxam and clothianidin in the total residues. Finally, the figure below shows data based on exposure to nectar only. Pollen would generally contribute only about 2% of the residue expression, so it was considered to have negligible impact on

residue concentrations. This data suggests that residues from soil applications of clothianidin to ornamental plants may be high enough to pose risk to foraging honey bees.

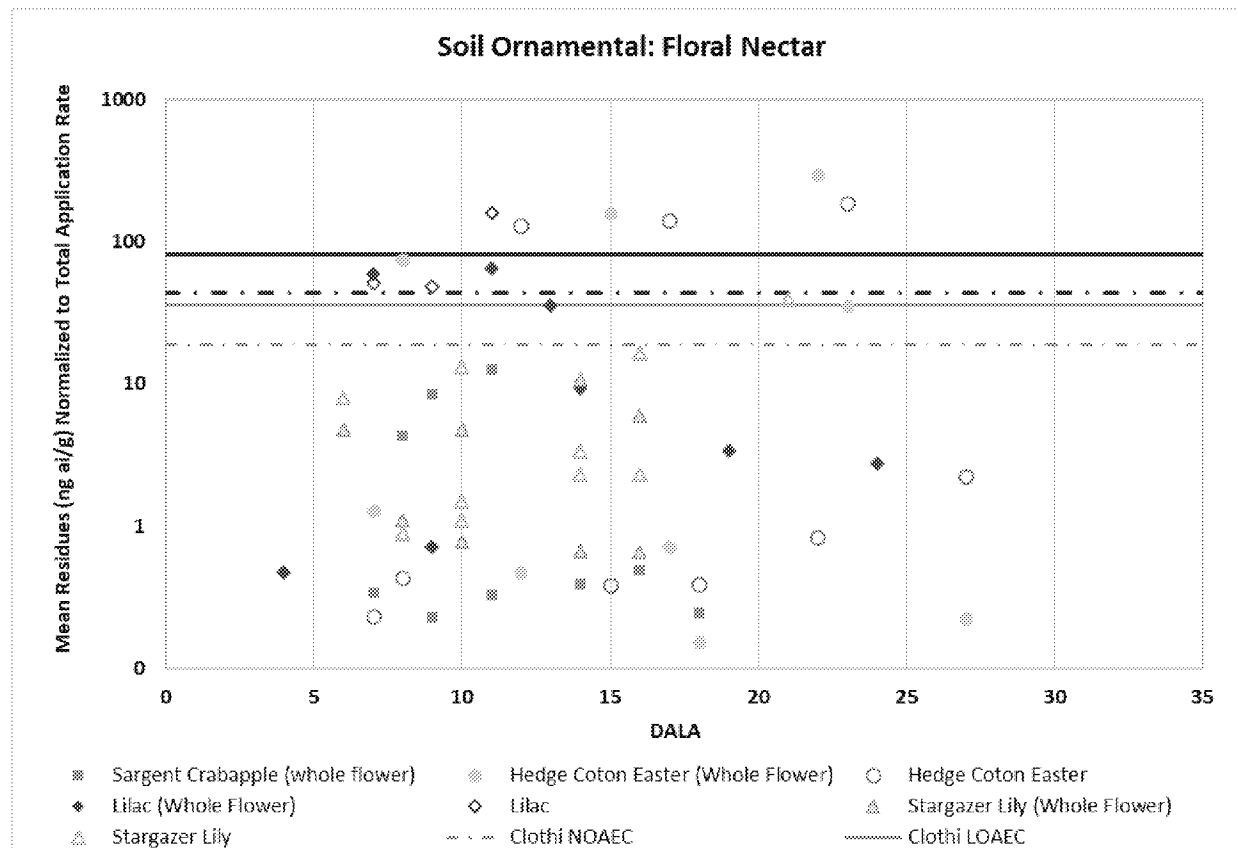


Figure [STYLEREf 1 \s]-33. Mean concentrations of thiamethoxam (in clothianidin equivalents adjusted to the maximum seasonal foliar rate of 0.266 lb a.i./A) in ornamental plant nectar (open symbols) and whole flowers (closed symbols) following soil application. Thicker red dashed and solid horizontal lines represent the thiamethoxam honey bee colony-level NOAEC and LOAEC (44 and 81 ng c.e./g, respectively). Thinner blue dashed and solid horizontal lines represent the clothianidin NOAEC and LOAEC endpoints (19 and 35.5 ng c.e./g, respectively) for comparison. Residues in whole flowers were converted to nectar equivalents by applying a conversion factor of 0.25x to the whole flower residue samples.

5.2.2.7.2 Turfgrass

Clothianidin and thiamethoxam are registered for applications commercial and residential turfgrass using a variety of methods including foliar spray and broadcast granular applications. The maximum single and seasonal application rate is 0.4 lb a.i./A for clothianidin and 0.266 lb c.e./A for thiamethoxam. Usage information is not available for residential or commercial turf uses of clothianidin and thiamethoxam. Although turfgrass itself is not attractive to honey bees and other non-*Apis* bees, flowering weeds such as clover and dandelions are commonly distributed within turfgrass and are considered attractive to bees. For residential turfgrass applications, the presence of flowering weeds

which are attractive to bees cannot be reasonably precluded, since weed control practices vary widely among homeowners and commercial lawn care practices. Therefore, a reasonable potential exists for exposure of bees to clothianidin applications to residential turfgrass.

No registrant-submitted residue data on clothianidin or thiamethoxam in blooming weeds associated with turfgrass application were available for assessing exposure to bees. However, an open literature study was available which quantified residues of clothianidin (and imidacloprid) in white clover following application to turfgrass (Larson *et al.* 2015). In their study, Larson *et al.* (2015) quantified residues of clothianidin in nectar of white clover following a single application of either 0.4 lb ai/A clothianidin (ARENA™ 50 WDG) or imidacloprid (MERIT™ 75 WSP) liquid formulation. Separate trials were conducted in June and August 2013 (4 replicates per trial) in which applications were made during bloom of clover in the turfgrass. Residues of clothianidin were measured in nectar 1 day after application and again 21 days later in newly blooming clover after mowing (**Table 5-39**). This study is classified for qualitative use in risk assessment due to lack of raw data for independent analysis.

Results from Larson *et al.* (2015) indicate relatively high levels of clothianidin residues occur in clover nectar 1 day after receiving direct foliar spray application (**Table 5-39**). Mean residues in 2 trials were approximately 3,000 ppb, which exceeds the colony-level NOAEC and LOAEC endpoints for clothianidin by approximately 100X (~40x~70x in comparison with the thiamethoxam endpoints). However, 21 days later, mean residues of clothianidin in nectar of newly blooming clover after mowing were lower (4-33 ppb) which range from below the clothianidin NOAEC of 19 ppb to almost exceeding the clothianidin LOAEC of 35.5 ppb. These later residues were below the thiamethoxam colony effect level endpoints. Since residues were not measured in between these sampling periods, the duration of time over which residues exceed of the NOAEC and LOAEC is not known with precision. Notably, concentrations of imidacloprid, applied at the same application rate as clothianidin, are within a factor of 2 of clothianidin during both sampling times. This finding suggests that the uptake and translocation of imidacloprid and clothianidin in white clover are comparable, which is consistent with their similar physicochemical and fate properties and provides further evidence that different neonicotinoids behave similarly in turfgrass, suggesting that these residues would be similar following thiamethoxam applications.

As an indication of the potential hazard of the clover nectar to bees, these authors conducted a subsequent bioassay by feeding this same nectar to the Insidious Flower Bug, *Orius insidiosus*. Honey bees were not used in the bioassay due to insufficient nectar volume. Results from their bioassay indicate a significantly increase in percent mortality of *O. insidiosus* (>90%) after 24 hours feeding on nectar which was collected 1-d after direct application. Mortality in controls was 20% after 24 hours. However, when *O. insidiosus* were fed nectar collected 21 days after application on newly blooming clover, mortality was not significantly different from controls (20-30%).

These results from the residue and bioassay measurements suggest that clothianidin and thiamethoxam residues in nectar of blooming weeds sampled immediately following foliar turfgrass application exceed levels associated with colony-level effects in honey bees. Acute toxicity was also noted on an insect species when fed this same nectar. However, the duration of exceedance of the clothianidin colony-level NOAEC is not known with precision, but appears to approximate 21 days or less when clover is mowed. Therefore, there is uncertainty when comparing these results to those of the colony-level feeding study which involved a 6-week exposure. For thiamethoxam, there is decreased certainty in the risk conclusions as the duration of exceedance is likely substantially less given the lower application rate and higher colony level endpoints. However, given the extremely high initial residues that are ~40x the thiamethoxam LOAEC, the thiamethoxam risk conclusions do not differ from the conclusions for

clothianidin despite the lower application rate and higher colony level effect endpoints. **Overall, there is moderate evidence indicating that use of both clothianidin and thiamethoxam on attractive flowering weed species presents potential risk to honey bee colonies.** This conclusion is also supported by limited incident information. A single beekill incident has been reported to the Agency following foliar application of clothianidin to sod grown on a sod farm. The legality of the use was not determined and the attribution of the incident to the use of clothianidin was determined to be probable, though it is unclear if the beekill was due to direct spray drift from the application or from foraging bees consuming contaminated nectar and pollen following the incident.

Table 5-39. Summary of imidacloprid and clothianidin residues in white clover nectar following foliar applications to turfgrass

Species	App Method	App rate	Application Timing	Measurement DALA	Concentration in Nectar (µg ai/kg) ⁽¹⁾	Concentration in Pollen (µg ai/kg)	Reference (Classification)
IMIDACLOPRID							
Kentucky Blue Grass & Tall Fescue with 30% White Clover (Trifolium repens)	Foliar	0.4 lb ai/A (MERIT 75 WSP)	June 3	1	5,493 ± 1040	NA	Larson et al. (2015) (Qualitative)
			Aug 15	1	6588 ± 752		
			June 3	21 (after mowing)	8.4 ± 2.2	NA	
			Aug 15	21 (after mowing)	26 ± 10		
CLOTHIANIDIN							
Kentucky Blue Grass & Tall Fescue with 30% White Clover (Trifolium repens)	Foliar	0.4 lb ai/A (ARENA 5 WDG)	June 3	1	2,992 ± 541	NA	Larson et al. (2015) (Qualitative)
			Aug 15	1	2882 ± 228		
			June 3	21 (after mowing)	6.2 ± 2.1	NA	
			Aug 15	21 (after mowing)	18 ± 15		

⁽¹⁾ mean \pm SE (n=4). Parent imidacloprid only

5.3 Higher Tier Analysis for Bumble Bees and Other Bee Species

For higher-tiered testing, collectively, potential effects on social non-*Apis* species were reported at the Tier II and III level from exposure to clothianidin at concentrations/doses lower than the registrant-submitted colony feeding studies with honey bees (MRIDs 49836101, 50312501, 50478501 – Clothianidin; 49757201, 50432101– Thiamethoxam), but not in all cases (Section 4, Appendices 3 and 4). This suggests that for uses with risk based on Tier II assessments, there are also risk concerns for other social species of bees, such as bumble bees. However, these studies have limitations, were classified as supplemental, and were used qualitatively as no process has been developed for quantifying risks to non-*Apis* species. As such, while there may be potential effects to non-*Apis* species, the ability to reliably determine a no-effect concentration is limited. As the pollinator risk assessment framework used by the EPA indicates the honey bees are intended to be reasonable surrogates for other bee species, conclusions from the weight of evidence for the honey bee can be used to help inform about potential risks to other non-*Apis* species.

The risk assessment for honey bees relies heavily on attractiveness of crops. The crops for which there are risk concerns for honey bee colonies would also be assumed to pose a risk to bumble bee colonies. There are some crops that are not attractive to honey bees, but are attractive to bumble bees, including additional crops in the fruiting vegetables and root and tuber crop groups. Since risk is identified to honey bee colonies for some crops in those groups (*e.g.*, sweet potatoes, chilis), risk to all bumble bee attractive crops in those groups would also be assumed.

6 Conclusions

6.1 Honey Bees

Tables 6.1 and 6.2 summarize the risk conclusions for honey bee colonies associated with each crop or crop group³² for which clothianidin and thiamethoxam (respectively) are registered. Conclusions are for on-field exposures and are expressed as red text indicate uses of clothianidin and thiamethoxam which pose risks to bees. Green text indicates cases where the likelihood of adverse effects on bees from a particular use is considered low. For those uses where there are risk concerns for colony level effects, the weight of evidence supporting the risk conclusion is characterized as either strongest, moderate or weakest.

Multiple lines of evidence were considered to evaluate risk conclusions, including: multiple residue values (total food) above colony level NOAEC and LOAEC, estimated median, 70th and 90th percentile residues above colony level NOAEC and LOAEC, duration of residues above colony level endpoints on the order of weeks, magnitude of residues relative to endpoints suggests that substantial dilution of residues from uncontaminated food sources would be needed to prevent colony-level effects. The majority of the analysis is based on three robust colony feeding studies (Tier II) submitted for clothianidin and thiamethoxam. Other supplemental/qualitative semi-field (Tier II) studies and full field (Tier III) studies were also considered as lines of evidence when available for a given use. Reported incidents were also considered.

³² Crops groups are codified in 40 CFR 180.41 and can be found here: <https://www.ir4project.org/crop-grouping/>

Robust residue data sets are available for foliar applications to the following bee attractive crops and crop groups: cotton, cucurbits, citrus, stone fruit, pome fruit, tree nuts, berries, soybeans and ornamentals. Robust residue data sets are available for soil applications to cucurbits, citrus, and berries. In general, residues from soil treatments are lower than those from foliar treatments and seed treatment residues are lower than those from soil applications. Residues for cotton and cucurbits are used as surrogates for other non-woody crops with limited or no residue data (*e.g.*, root and tubers, mint). Residues for stone fruit, pome fruit and citrus are used for other woody crops (*e.g.*, tree nuts, tropical fruits).

In general, if a crop is attractive to bees and there is potential for exposure, on field risk is expected from pre-bloom, foliar applications. The on-field risk from soil applications varies by use. In general, soil treatments pose a low risk; however, there are some limited exceptions. For uses with risk, the weight of evidence is characterized in terms of its robustness.

Uses with Low On-Field Risk:

This assessment concludes that the following crops and crop groups pose a low risk to honey bees because they are harvested prior to bloom (according to USDA 2017) and have limited on-field exposure to bees: bulb, leafy and brassica leafy vegetables; artichoke and tobacco. Therefore, any type of applications (*i.e.*, foliar, soil or seed) to these crops would pose a low on-field risk to bees. For these crops, one exception would be cases where the crop is grown for seed, thus, the crop would not be harvested prior to bloom. Although clothianidin and/or thiamethoxam may be applied to crops grown for seed, the spatial footprint for these uses is expected to be limited due to low pounds applied and specific geographic areas where crops are grown for seed.

This assessment concludes that the following crops and crop groups pose a low risk to honey bees because they are not attractive to honey bees (according to USDA 2017) and have limited on-field exposure to honey bees: root and tuber vegetables (except sweet potato, Jerusalem artichoke, edible burdock, dasheen and horseradish), fruiting vegetables (except roselle, okra, chilies and peppers). Therefore, any type of applications (*i.e.*, foliar, soil or seed) to these crops would pose a low on-field risk to honey bees.

For crops where clothianidin or thiamethoxam are applied as seed treatment, there is a low risk from exposures of clothianidin and thiamethoxam to honey bees. These conclusions are based on available empirical residue data for seed treated crops (*i.e.*, corn, cotton, canola and soybeans) and bridging to other crops receiving seed treatments. Although the default BeeREX RQs are above LOCs, the majority of refined RQs (with empirical residues) are below LOCs. For clothianidin, the following uses had refined Tier I RQs above the LOCs for adult bees: canola, cereal grains, legumes, sorghum and soybeans. When residues were compared to the Tier II honey bee colony endpoints, residues were all below the NOAEC, indicating low risk of colony level effects. For thiamethoxam, the following uses had refined Tier 1 RQs above the LOC for adult bees: beans, cucurbits, legumes, lentils, peanuts, peas, sorghum, soybeans and sunflower. All uses had residues below the clothianidin and thiamethoxam colony level NOAEC (both are considered because both chemicals are part of thiamethoxam's residues of concern), except for cucurbits. The weight of evidence indicates a low risk from thiamethoxam seed treatments to cucurbits. In summary, a low risk conclusion is made for on field exposures associated with all clothianidin and thiamethoxam seed treatment uses, except clothianidin applications to turmeric seed pieces (discussed below).

Low risk conclusions are also made for several foliar or soil uses because residues were below colony level endpoints. This applies to the following crops (or groups):

- Foliar applications of clothianidin and thiamethoxam to soybeans;
- Foliar, post-bloom applications of clothianidin and thiamethoxam to orchard crops;

[PAGE * MERGEFORMAT]

- Foliar and soil, post-bloom applications of clothianidin and thiamethoxam to berries;
- Soil, pre-bloom applications of clothianidin to grapes.

Uses With On-Field Risk and Strongest Evidence of Risk:

The strongest evidence of risk is represented by cases where assumptions related to exposure and effects are not expected to have a major influence on risk conclusions and there are multiple lines of evidence indicating the potential for effects to honey bee colonies. A strong evidence of risk may be represented by a case where many measured residues for the crop of interest exceed both the colony level LOAEC and NOAEC for a relatively long duration (*e.g.*, several weeks). Residues that are an order of magnitude above CFS endpoints (indicating that only a small fraction of the honey bee colony's nectar and pollen need to be from treated fields); and the observation that multiple locations in the residue trials and/or multiple crops within the crop group yielded residues above CFS endpoints. In addition, incident reports of bee kills (*i.e.*, for clothianidin use on cotton; for thiamethoxam use in orchards) may provide additional lines of evidence for a strong evidence of risk conclusion. The following uses represent a risk to honey bee colonies and have the strongest weights of evidence.

- For Clothianidin:
 - o Foliar applications to cotton;
 - o Foliar and soil applications to cucurbits;
 - o Foliar, pre-bloom applications to grapes.
- For Thiamethoxam:
 - o Foliar applications to cotton;
 - o Foliar applications to cucurbits;
 - o Foliar, pre-bloom applications to orchard crops (*i.e.*, citrus; pome, stone and tropical fruits; tree nuts);
 - o Soil, pre-bloom applications to citrus;
 - o Foliar and soil, pre-bloom applications to berries; and
 - o Foliar applications to honey bee attractive fruiting vegetables (*i.e.*, okra, roselle, chilis and peppers).

Uses with On Field Risk and Moderate Evidence of Risk:

The uses listed in this section are identified as posing a risk to honey bee colonies. These uses have a moderate weight of evidence, due to varying reasons (*e.g.*, not all lines of evidence suggest risk, or there are some uncertainties associated with the data that can influence the risk conclusion). Similar to above, multiple lines of evidence were considered to evaluate risk conclusions, including: multiple residue values (total food) above colony level NOAEC and LOAEC, duration of residues above colony level endpoints on the order of weeks, magnitude of residues relative to endpoints and incident reports.

The following uses represent a risk to honey bee colonies and have moderate weights of evidence:

- Clothianidin and Thiamethoxam:
 - o Soil, post-bloom applications to citrus;
 - o Foliar applications to residential lawns; and
 - o Foliar and soil applications to ornamentals.
- Thiamethoxam only:
 - o Soil applications to honey bee attractive fruiting vegetables; and
 - o Soil applications to cucurbits.

Uses with On Field Risk and Weakest Evidence of Risk:

The weakest evidence of risk is represented by cases where there is evidence to suggest colony level effects; however, it is not well supported by measured residue data for the chemical of interest. The following uses represent a risk to honey bee colonies and have the weakest weights of evidence:

- Clothianidin
 - o Foliar and soil applications to honey bee attractive root and tuber crops (*i.e.*, sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish); and
 - o Seed treatment to turmeric.
- Thiamethoxam
 - o Foliar and soil applications to honey bee attractive root and tuber crops;
 - o Foliar applications to mint.

For thiamethoxam applications (foliar) to mint and for clothianidin seed treatments to turmeric (seed pieces), the evidence is considered weakest because risk findings rely exclusively on residue data that are extrapolated (bridged) from other neonicotinoids or different crop groups where the influence of crop on the magnitude of the residue is highly uncertain.

For clothianidin and thiamethoxam applications to honey bee attractive root and tuber crops, the evidence is considered weakest because of the following. Residue data are available for potato pollen for clothianidin; however, this crop does not produce nectar, but other crops in the group do (*e.g.*, sweet potatoes). Residues in potato pollen are below the colony level endpoints; however, it cannot be concluded that honey bee attractive root and tuber crops pose a low risk because there are no residue data for nectar. When considering residue data for other field crops (*e.g.*, cotton, cucurbits), foliar and soil applications result in residues in nectar that are above the colony level endpoints. This suggests a potential concern.

Off Site Risk Conclusions:

Based on a Tier I analysis, for foliar applications, off-field dietary risks to individual bees exposed to spray drift extend 1000 feet from the edge of the treated field. There is uncertainty in this conclusion which includes: assumption of available attractive forage off field, individual level toxicity data, BeeREX default estimates for residues, and AgDRIFT™ modeling.

Soil applications are assumed to have a low off-field risk because of low potential to drift.

In regard to seed treatments, there are risk concerns for potential off-site transport of contaminated dust at the time of planting. This concern is supported by multiple bee kill incidents for both clothianidin and thiamethoxam that are associated with the planting of treated seed, in particular corn.

Additionally, soil amendments of clothianidin-treated poultry litter (from the use in poultry houses) also pose a risk when applied to fields with honey bee attractive plants (*e.g.*, pasture).

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Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Summary of on-field risk findings for honey bee colonies (*Apis mellifera*) for the registered use patterns of clothianidin.

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data available? (quant)	Individual Bee Risk? (Tier I; Default)	Individual Bee Risk? (Tier I; Refined)	Honey Bee Colony Risk (Tier II)?	Risk Conclusions ^{2,3}
1	Root and Tuber Vegetables	Yes ⁵	Foliar	Potato (pollen-only)	Yes	Yes	Yes	RISK: Weakest
			Soil	Potato (pollen-only)	Yes	Yes	Yes	RISK: Weakest
			Seed	No	Yes	NA	No (except turmeric)	RISK: Weakest Turmeric only
		No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed	No	NA ³	NA	NA	LOW ⁴
3	Bulb Vegetables	No	Seed	No	NA ³	NA	NA	LOW ⁴
4	Leafy Vegetables	No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed	No	NA ³	NA	NA	LOW ⁴
5	Brassica Leafy Vegetables	No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed	No	NA ³	NA	NA	LOW ⁴
6	Legume Vegetables	Yes	Foliar (Soybean-only)	No	Yes	NA	No	LOW
			Seed	Soybean (qualitative)	Yes	Yes	No	LOW
9	Cucurbit Vegetables	Yes	Foliar	Pumpkin	Yes	Yes	Yes	RISK: Strongest
			Soil	Cucumber Pumpkins Squash Melon	Yes	Yes	Yes	RISK: Strongest
10	Citrus Fruits ⁶	No	No	NA ⁵	NA ³	NA	NA	LOW
		Yes	Post-bloom; Soil	Orange, Lemon	Yes	Yes	Yes	RISK: Moderate

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data available? (quant)	Individual Bee Risk? (Tier I; Default)	Individual Bee Risk? (Tier I; Refined)	Honey Bee Colony Risk (Tier II)?	Risk Conclusions ^{2,3}
11	Pome Fruits	Yes	Foliar: post-bloom	Apple	Yes	Yes	No	LOW
12	Stone Fruits	Yes	Foliar: post-bloom	Peaches	Yes	Yes	No	LOW
13	Berry and Small Fruit	Yes	Foliar: Pre-bloom (Grape, only)	Grape (pollen-only)	Yes	Yes	Yes	RISK: Strongest
			Foliar: Post-Bloom	Grape (pollen-only)	Yes	Yes	No	LOW
			Soil: Pre-bloom (Grape, only)	Grape (pollen-only)	Yes	Yes	No	LOW
			Soil: Post-bloom	None	Yes	NA	NA	LOW
14	Tree Nuts	Yes	Foliar: Post-bloom	No	Yes	Yes	No	LOW
15	Cereal Grains	No	Foliar (rice-only)	No	NA ³	NA	NA	LOW ⁴
		Yes	Soil (corn-only)	Corn	Yes	Yes	No	LOW
			Seed	Corn	Yes	Yes	No	LOW
20	Oilseed	Yes	Foliar: Cotton-only	Cotton	Yes	Yes	Yes	RISK: Strongest
			Seed	Cotton Canola	Yes	No	No	LOW
23	Tropical and Subtropical Fruit	No	Foliar: post bloom (Figs-only)	No	NA ³	NA	No	LOW
24	Tropical and Subtropical Fruit	Unknown	Foliar: post bloom (Pomegranate-only;)	No	Yes	NA	Yes	LOW
None	Artichoke	No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No		NA	NA	LOW ⁴

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data available? (quant)	Individual Bee Risk? (Tier I; Default)	Individual Bee Risk? (Tier I; Refined)	Honey Bee Colony Risk (Tier II)?	Risk Conclusions ^{2,3}
	Tobacco	No	Foliar	No	NA ³	NA	No	LOW ⁴
			Soil	No	NA ³	NA	No	LOW ⁴
	Sod	No	Foliar	No	NA ³	NA	NA	LOW ⁴
	Turf/Lawns	Yes	Foliar	No	Yes	NA	NA	RISK: Moderate ⁵
	Ornamentals	Yes	Foliar	No	Yes	NA	Yes	RISK: Moderate
			Soil	No	Yes	NA	Yes	RISK: Moderate
	Other outdoor residential uses ¹⁰	No	Spray	No	NA ³	NA	NA	LOW ⁴

NA = not assessed.

¹Based on USDA. 2017. Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen.

²Green indicates low risk; red indicates risk.

³If crop is not attractive to bees or is harvested prior to bloom (USDA 2017), RQs are not calculated and risk conclusion is "LOW."

⁴For uses where the crop is grown for food, roots, tubers, bulbs and/or leaves and are harvested prior to bloom (USDA 2017). This limits exposure to bees on field, as the crop is not attractive to bees when not flowering. Exposure may occur on the treated field if crop is grown for seed (*i.e.*, the crop is allowed to flower). Although clothianidin may be applied to crops grown for seed, the spatial footprint for these uses is expected to be limited due to low pounds applied and specific geographic areas where crops are grown for seed.

⁵Honey bee attractive crops with no indication of whether they are harvested prior to bloom (USDA 2017) in the root and tuber vegetable crop group include: sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish.

⁶No national registrations present, only Section 18 registrations in Florida and Texas.

⁷Residue data from other field crops across all four N-nitroguanidine group neonicotinoids (*i.e.*, clothianidin, dinotefuran, imidacloprid and thiamethoxam) used for exposure analysis (including cucurbits, fruiting vegetables).

⁸It is assumed that bee-attractive, blooming weeds (*e.g.*, clover, dandelions) may be present on treated lawns

⁹Residue data were pre-bloom. Labels do not have pre-bloom restriction; therefore, no distinction is made between risk calls for pre- and post-bloom applications.

¹⁰Crack and crevice treatments, perimeter treatment of buildings, etc.

Table [STYLEREf 1 \s]-[SEQ Table * ARABIC \s 1]. Summary of on-field risk findings for honey bee colonies (*Apis mellifera*) for the registered use patterns of thiamethoxam.

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data available? (quant)	Individual Bee Risk? (Tier I; Default)	Individual Bee Risk? (Tier I; Refined)	Honey Bee Colony Risk? (Tier II)	Risk Conclusions ^{2,3}
1		Yes ⁵	Foliar	No	Yes	Yes	Yes	RISK: Weakest

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data available? (quant)	Individual Bee Risk? (Tier I; Default)	Individual Bee Risk? (Tier I; Refined)	Honey Bee Colony Risk? (Tier II)	Risk Conclusions ^{2,3}
	Root and Tuber Vegetables	No	Soil	No	Yes	Yes	Yes	RISK: Weakest
			Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed (carrot, potato, sugar beet only)	No	NA ³	NA	NA	LOW ⁴
3	Bulb Vegetables	No	Seed	No	NA ³	NA	NA	LOW ⁴
4	Leafy Vegetables	No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed	No	NA ³	NA	NA	LOW ⁴
5	Brassica Leafy Vegetables	No	Foliar	No	NA ³	NA	NA	LOW ⁴
			Soil	No	NA ³	NA	NA	LOW ⁴
			Seed	No	NA ³	NA	NA	LOW ⁴
6	Legume Vegetables	Yes	Foliar (soybean only)	Soybean	Yes	Yes	No	LOW ⁴
			Seed (soybean only)	Soybean	Yes	Yes	No	LOW
8	Fruiting Vegetables	Yes ⁶	Foliar	No	Yes	Yes	Yes	RISK: Strongest
			Soil	Pepper Tomato	Yes	Yes	Yes	RISK: Moderate
		No	Foliar	Tomato	NA ³	NA	NA	LOW ⁴
			Soil	No	Yes	NA	NA	LOW ⁴
9	Cucurbit Vegetables	Yes	Foliar	Cucumber Pumpkin	Yes	Yes	Yes	RISK: Strongest
			Soil	Cucumber Pumpkins Squash Melon	Yes	Yes	Yes	RISK: Moderate
			Seed	No	Yes	Yes	No	LOW
10	Citrus Fruits	No ⁷	No	No	NA ³	NA	NA	LOW
		Yes	Foliar: Pre-bloom	No	Yes	Yes	Yes	RISK: Strongest

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data available? (quant)	Individual Bee Risk? (Tier I; Default)	Individual Bee Risk? (Tier I; Refined)	Honey Bee Colony Risk? (Tier II)	Risk Conclusions ^{2,3}
			Foliar: Post-bloom	No	Yes	Yes	No	LOW
			Soil: Pre-bloom	Orange Lemon	Yes	Yes	No	RISK: Strongest
			Soil: Post-bloom	Orange	Yes	Yes	No	RISK: Moderate
11	Pome Fruits	Yes	Foliar: Pre-bloom	Apple	Yes	Yes	Yes	RISK: Strongest
			Foliar: Post-bloom	No	Yes	Yes	No	LOW
12	Stone Fruits	Yes	Foliar: pre-bloom	No	Yes	Yes	Yes	RISK: Strongest
			Foliar: post-bloom	Peach Plum Cherry	Yes	Yes	No	LOW
13	Berry and Small Fruit	Yes	Foliar: pre-bloom	Blueberry Cranberry Strawberry	Yes	Yes	Yes	RISK: Strongest
			Foliar: post-bloom	No	Yes	Yes	Yes	LOW
			Soil: pre-bloom	Strawberry	Yes	Yes	Yes	RISK: Strongest
			Soil: post-bloom	No	Yes	Yes	Yes	LOW
14	Tree Nuts	Yes	Foliar: Pre-bloom	No	Yes	Yes	Yes	RISK: Strongest
			Foliar: Post-bloom	No	Yes	Yes	No	LOW
15	Cereal Grains	No	Foliar (Barley only)	No	NA ³	NA	NA	LOW ⁴
		Yes	Seed	Corn	Yes	No	NA	LOW
18	Forage Fodder, Straw and Hay	Yes	Seed (alfalfa only)	No	Yes	Yes	No	LOW
19	Herbs and Spices	Yes	Foliar (mint only)	No	Yes	Yes	Yes	RISK: Weakest ⁵

Group #	Crop Group	Honey Bee attractive? ¹	Appl. Method	Residue data available? (quant)	Individual Bee Risk? (Tier I; Default)	Individual Bee Risk? (Tier I; Refined)	Honey Bee Colony Risk? (Tier II)	Risk Conclusions ^{2,3}
20	Oilseed	Yes	Foliar (cotton only)	Cotton	Yes	Yes	Yes	RISK: Strongest
			Seed	Cotton Canola	Yes	No	No	LOW
23 & 24	Tropical and Subtropical Fruit	Yes	Foliar: Pre-bloom	No	Yes	Yes	Yes	RISK: Strongest
			Foliar: Post-bloom	No	Yes	Yes	No	LOW
None	Artichoke	No	Foliar	No	NA ³	NA	NA	LOW ⁴
	Tobacco	No	Foliar	No	NA ³	NA	NA	LOW ⁴
	Peanuts	Yes	Seed	No	Yes	Yes	No	LOW
	Sod	No	Foliar	No	NA ³	NA	NA	LOW ⁴
	Turf/Lawns	Yes ⁹	Foliar	No	Yes	NA	NA	RISK: Moderate ₉
	Ornamentals	Yes	Foliar ¹⁰	Stargazer Lily Mock Orange Lilac	Yes	Yes	Yes	RISK: Moderate
			Soil ¹⁰	Hedge Cotoneaster Lilac Sargeant Crabapple	Yes	Yes	Yes	RISK: Moderate
	Christmas tree plantation	No	Soil	No	NA ³	NA	NA	LOW ⁴
	Other outdoor residential uses ¹¹	No	Spray	No	NA ³	NA	NA	LOW ⁴

NA = not assessed.

¹Based on USDA. 2017. Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen.

²Green indicates low risk; red indicates risk.

³If crop is not attractive to bees or is harvested prior to bloom, RQs are not calculated and risk conclusion is "LOW."

⁴For uses where the crop is grown for food, roots, tubers, bulbs and/or leaves and are harvested prior to bloom (USDA 2017). This limits exposure to bees on field, as the crop is not attractive to bees when not flowering. Exposure may occur on the treated field if crop is grown for seed (*i.e.*, the crop is allowed to flower).

Although thiamethoxam may be applied to crops grown for seed, the spatial footprint for these uses is expected to be limited due to low pounds applied and specific geographic areas where crops are grown for seed.

⁵Honey bee attractive crops with no indication of whether they are harvested prior to bloom (USDA 2017) in the root and tuber vegetable crop group include: sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish.

⁶Honey bee-attractive crops in the fruiting vegetable crop group include: roselle, okra and chilies and peppers (USDA 2017).

⁷During bloom, mandarin orange trees are tented with nets to prevent bees from pollinating their flowers.

⁸Residue data from other field crops used for exposure analysis (including cucurbits, fruiting vegetables).

⁹It is assumed that bee-attractive, blooming weeds (*e.g.*, clover, dandelions) are present on treated lawns.

¹⁰Residue data were pre-bloom. Labels do not have pre-bloom restriction; therefore, no distinction is made between risk calls for pre- and post-bloom applications.

¹¹Crack and crevice treatment of patios, perimeter treatment of buildings, and barrier treatments of garbage cans.

6.2 Bumble bees and other species of bees

Comparisons of available Tier I toxicity data for non-*Apis* species, including bumble bees indicates that honey bees are of similar sensitivity to clothianidin and thiamethoxam to other species of bees. An analysis of food consumption rates (of pollen and nectar) for several species of bees suggests that honey bees are similar or protective of other species. Therefore, honey bees represent an appropriate surrogate for assessing individual level risks to other species of bees. Therefore, tier I conclusions for honey bees are also used to represent risks to solitary bees. One notable exception relates to differences in attractiveness of crops. It should be noted that many of the fruiting vegetables are not attractive to honey bees but are attractive other species of bees (*e.g.*, *Bombus* sp). Therefore, additional crops in the fruiting vegetables group that were considered low risk to honey bees may pose a risk to non-*Apis* bees.

For higher-tiered testing, collectively, potential effects on social non-*Apis* species were reported at the Tier II and III level from exposure to clothianidin at concentrations/doses lower than the registrant-submitted colony feeding studies with honey bees (MRIDs 49836101, 50312501, 50478501 – Clothianidin; 49757201, 50432101– Thiamethoxam), but not in all cases. This suggests that for uses with risk based on Tier II assessments, there are also risk concerns for other social species of bees, such as bumble bees. However, these studies have limitations, were classified as supplemental, and were used qualitatively as no process has been developed for quantifying risks to non-*Apis* species. As such, while there may be potential effects to non-*Apis* species, the ability to reliably determine a no-effect concentration is limited. As the pollinator risk assessment framework used by the EPA indicates the honey bees are intended to be reasonable surrogates for other bee species, conclusions from the weight of evidence for the honey bee can be used to help inform about potential risks to other non-*Apis* species.

7 References

Abbott VA, Nadeau JL, Higo HA and Winston ML. 2008. Lethal and sublethal effects of imidacloprid on *Osmia lignaria* and clothianidin on *Megachile rotundata* (Hymenoptera: Megachilidae). J Econ Entomol 101(3):784-796.

Alarcón AL, Cánovas M, Senn R and Correia R. 2005. The safety of thiamethoxam to pollinating bumble bees (*Bombus terrestris* L.) when applied to tomato plants through drip irrigation. Commun Agric Appl Biol Sci 70(4):569-579.

Aliouane Y, El Hassani AK, Gary V, Armengaud C, Lambin M and Gauthier M. 2009. Subchronic exposure of honeybees to sublethal doses of pesticides: Effects on behavior. Environ Toxicol Chem 28(1):113-122.

Arena, M. and F. Sgolastra. 2014. A meta-analysis comparing the sensitivity of bees to pesticides. Ecotoxicology 23: 324 – 334.

Bailey J, Scott-Dupree C, Harris R, Tolman J and Harris B. 2005. Contact and oral toxicity to honey bees (*Apis mellifera*) of agents registered for use for sweet corn insect control in Ontario, Canada. Apidologie 36(4):623-633.

Boily M, Sarrasin B, DeBlois C, Aras P and Chagnon M. 2013. Acetylcholinesterase in honey bees (*Apis mellifera*) exposed to neonicotinoids, atrazine and glyphosate: Laboratory and field experiments. Environ Sci Pollut Res 20(8):5603-5614.

Catae AF, Roat TC, De Oliveira RA, Ferreira Nocelli RC and Malaspina O. 2014. Cytotoxic effects of thiamethoxam in the midgut and malpighian tubules of Africanised *Apis mellifera* (Hymenoptera: *Apidae*). *Microsc Res Tech* 77:274-281.

Chandramani P, Rani BU, Muthiah C, Kumar S. 2008. Evaluation of toxicity of certain insecticides to India honeybee, *Apis cerana indica* F. *Pestology* 32(8):42-43.

Cutler GC, Scott-Dupree CD, Sultan M, McFarlane AD, Brewer L. 2014. A large-scale field study examining effects of exposure to clothianidin seed-treated canola on honey bee colony health, development, and overwintering success. *Peerj* 2:e652.

Elston C, Thompson HM and Walters KFA. 2013. Sub-lethal effects of thiamethoxam, a neonicotinoid pesticide, and propiconazole, a DMI fungicide, on colony initiation in bumblebee (*Bombus terrestris*) micro-colonies. *Apidologie* 44(5):563-574.

Fausser-Misslin A, Sadd BM, Neumann P and Sandrock C. 2013. Influence of combined pesticide and parasite exposure on bumblebee colony traits in the laboratory. *J Appl Ecol* 51:450-459.

Forster, R. 2009. Bee poisoning caused by insecticidal seed treatment of maize in Germany in 2008. Pages 126 – 131 *in* P. A. Oomen and H. M. Thompson (editors) *Hazards of Pesticides to Bees*, 10th International Symposium of the ICP-BR Bee Protection Group, Bucharest (Romania), October 8 – 10, 2008. *Julius Kühn Arch* 423.

Girolami V., L. Mazzon, A. Squartini, N. Mori, and M. Marzaro, A. Di Bernardo, M. Greatti, C. Giorio and A. Tapparo. 2009. Translocation of Neonicotinoid Insecticides from Coated Seeds to Seedling Guttation Drops: A Novel Way of Intoxication for Bees. *Journal of Economic Entomology*, 102(5): 1808-1815. MRID 48077913.

Godfray HCJ, Blacquière T, Field LM, Hails RS, Petrokofsky G, Potts SG, Raine NE, Vanbergen AJ, McLean AR. 2014. A restatement of the natural science evidence base concerning neonicotinoid insecticides and insect pollinators. *Proc. R. Soc. B* 281: 20140558.

Henry M, Béguin M, Requier F, Rollin O, Odoux J-, Aupinel P, Aptel J, Tchamitchian S and Decourtye A. 2012. A common pesticide decreases foraging success and survival in honey bees. *Science* 336(6079):348-350.

Iwasa T, Motoyama N, Ambrose JT and Roe RM. 2004. Mechanism for the differential toxicity of neonicotinoid insecticides in the honey bee, *Apis mellifera*. *Crop Protection* 23(5):371-378.

Kessler, Sebastien C.; Tiedeken, Erin Jo; Simcock, Kerry L.; Derveau, Sophie; Mitchell, Jessica; Softley, Samantha; Stout, Jane C.; Wright, Geraldine A.. 2015. Bees prefer foods containing neonicotinoid pesticides. *Letter. Nature*. 1, 00 month 2015, vol 000

Krupke, C. H., G. J. Hunt, B. D. Eitzer, G. Andino, K. Given. 2012. Multiple routes of pesticide exposure for honey bees living near agricultural fields. *PLoS ONE* 7(1): e29268. Doi:10.1371/journal.pone.0029268

Larson JL, Redmond CT and Potter DA. 2013. Assessing insecticide hazard to bumble bees foraging on flowering weeds in treated lawns. *Plos One* 8(6):e66375.

Laurino D, Manino A, Patetta A, Ansaldi M and Porporato M. 2010. Acute oral toxicity of neonicotinoids on different bee strains. *Redia*; 2010.93:99-102.

Laurino D, Porporato M, Patetta A and Manino A. 2011. Toxicity of neonicotinoid insecticides to honey bees: Laboratory tests. *Bull Insect* 64(1):107-113.

Laurino D, Manino A, Patetta A and Porporato M. 2013. Toxicity of neonicotinoid insecticides on different honey bee genotypes. *Bull Insect* 66(1):119-126.

Laycock I, Cotterell KC, O'Shea-Wheller TA and Cresswell JE. 2014. Effects of the neonicotinoid pesticide thiamethoxam at field-realistic levels on microcolonies of *Bombus terrestris* worker bumble bees. *Ecotoxicology and Environmental Safety* 100:153-158.

Lu, Chensheng et al. 2015. Distributions of neonicotinoid insecticides in the Commonwealth of Massachusetts: a temporal and spatial variation analysis for pollen and honey samples. *Environmental Chemistry*. [tp://dx.doi.org/10.1071/EN15064](http://dx.doi.org/10.1071/EN15064).

Matsumoto T. 2013. Reduction in homing flights in the honey bee *Apis mellifera* after a sublethal dose of neonicotinoid insecticides. *Bulletin of Insectology* 66(1):1-9.

Mullin CA, Frazier M, Frazier JL, Ashcraft S, Simonds R, et al. (2010) High Levels of Miticides and Agrochemicals in North American Apiaries: Implications for Honey Bee Health. *PLoS ONE* 5(3): e9754. doi:10.1371/journal.pone.0009754

OECD (2013), *Test No. 237: Honey Bee (Apis Mellifera) Larval Toxicity Test, Single Exposure*, OECD Publishing, Paris. DOI: [[HYPERLINK "http://dx.doi.org/10.1787/9789264203723-en"](http://dx.doi.org/10.1787/9789264203723-en) \h]

Oliveira RA, Roat TC, Carvalho SM and Malaspina O. 2013. Side-effects of thiamethoxam on the brain and midgut of the Africanized honeybee *Apis mellifera* (Hymenoptera: Apidae). *Environ Toxicol* 13(4).

Pistorius, J., G. Bischoff, U. Heimbach, and M. Stähler. 2009. Bee poisoning incidents in Germany in spring 2008 caused by abrasion of active substance from treated seeds during sowing of maize. Pages 118 – 126 in P. A. Oomen and H. M. Thompson (editors) *Hazards of Pesticides to Bees, 10th International Symposium of the ICP-BR Bee Protection Group, Bucharest (Romania), October 8 – 10, 2008*. Julius Kühn Arch 423

Pohorecka K, Skubida P, Semkiw P, Miszczak A, Teper D, Sikorski P, Zagibajlo K, Skubida M, Zdańska D and Bober A. 2013. Effects of exposure of honey bee colonies to neonicotinoid seed- treated maize crops. *J Apic Sci* 57(2):199-208.

Rundlöf M., Andersson G.K.S., Bommarco R., Fries I., Hederström V., Herbertsson L., Jonsson O., Klatt B.K., Pedersen T.R., Yourstone J., Smith H.G. 2015. Seed coating with a neonicotinoid insecticide negatively affects wild bees. *Nature* 521, 77–80

Sandrock, C., L. G. Tanadini, J. S. Pettis, J. C. Biesmeijer, S. G. Potts, P. Neumann. 2014a. Sublethal neonicotinoid insecticide exposure reduces solitary bee reproductive success. *Agricultural and Forest Entomology*, 16: 119-128.

Sandrock C, Tanadini M, Tanadini LG, Fauser-Misslin A, Potts SG and P. Neumann. 2014b. Impact of Chronic Neonicotinoid Exposure on Honeybee Colony Performance and Queen Superseding. PLoS ONE 9(8): e103592. doi:10.1371/journal.pone.0103592.

Schneider CW, Tautz J, Grünewald B and Fuchs S. 2012. RFID tracking of sublethal effects of two neonicotinoid insecticides on the foraging behavior of *Apis mellifera*. Plos One 7(1):e30023.

Scholer J, Krischik V (2014) Chronic Exposure of Imidacloprid and Clothianidin Reduce Queen Survival, Foraging, and Nectar Storing in Colonies of *Bombus impatiens*. PLoS ONE 9(3): e91573.

Scott-Dupree CD, Conroy L, Harris CR. 2009. Impact of currently used or potentially useful insecticides for canola agroecosystems on *Bombus impatiens* (Hymenoptera: Apidae), *Megachile rotundata* (Hymenoptera: Megachilidae), and *Osmia lignaria* (Hymenoptera: Megachilidae). J Econ Entomol 102(1):177-182.

Sechser B, Reber B, Freuler J. 2002. The safe use of thiamethoxam by drench or drip irrigation in glasshouse crops where bumble bees *Bombus terrestris* (L.) are released. Mitteilungen Der Schweizerischen Entomologischen Gesellschaft 75(3/4):273-287.

Stanley DA, Garratt MP, Wickens JB, Wickens VJ, Potts SG, Raine NE. 2015. Neonicotinoid pesticide exposure impairs crop pollination services provided by bumblebees. Nature 528, 548– 550 (24 December 2015)

Stoner KA., Eitzer BD., 2012. Movement of Soil-Applied Imidacloprid and Thiamethoxam into Nectar and Pollen of Squash (*Cucurbita pepo*). PLoS One, 7:6. PMID 22719616.

Stoner KA, Eitzer BD (2013) Using a Hazard Quotient to Evaluate Pesticide Residues Detected in Pollen Trapped from Honey Bees (*Apis mellifera*) in Connecticut. PLoS ONE 8(10): e77550. doi:10.1371/journal.pone.0077550

Tapparo, A., D. Marton, C. Giorio, A. Zanella, L. Soldà, M. Marzaro, L. Vivan, V. Girolami. 2012. Assessment of the environmental exposure of honey bees to particulate matter containing neonicotinoid insecticides coming from corn coated seeds. Environmental Science and Technology 46: 2592 - 2599.

Tavares, Daiana Antonia; Roat, Thaisa Cristina; Carvalho, Stephan Malfitano; Silva-Zacarin, Elaine Cristina Mathias; Malaspina, Osmar. 2015. In vitro effects of thiamethoxam on larvae of Africanized honey bee *Apis mellifera* (Hymenoptera: Apidae).. Chemosphere 135 (2015) 370–378

Thomazoni D, Soria MF, Kodama C, Carbonari V, Fortunato RP, Degrande PE and Valter Junior VA. 2009. Selectivity of insecticides for adult workers of *Apis mellifera* (Hymenoptera: Apidae). Revista Colombiana De Entomologia 35(2):173-176.

Thompson HM, Fryday SL, Harkin S, Milner S. 2014. Potential impacts of synergism in honeybees (*Apis mellifera*) of exposure to neonicotinoids and sprayed fungicides in crops. Apidologie 45(5):545-553.

Thompson, H. 2016. Extrapolation of Acute Toxicity Across Bee Species. Integrated Environmental Assessment and Management 12(4): 622 -626

Thompson,H.;Coulson,M.;Ruddle,N.;Wilkins,S.;Harkin,S.. 2016b. Thiamethoxam: Assessing flight activity of honeybees foraging on treated oilseed rape using radio frequency identification technology. Environmental Toxicology and Chemistry, Vol. 35, No. 2, pp. 385–393, 2016

Tomizawa, M, Casida, J. 2005. Neonicotinoid insecticide toxicology: mechanisms of Selective Action. Annual Review of Pharmacology and Toxicology, 45, 247–268.

USDA. 2014. Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen. (available at: [HYPERLINK

"http://www.ree.usda.gov/ree/news/Attractiveness_of_Agriculture_crops_to_pollinating_bees_Report-FINAL.pdf" \h] [HYPERLINK

"http://www.ree.usda.gov/ree/news/Attractiveness_of_Agriculture_crops_to_pollinating_bees_Report-FINAL.pdf" \h]

Tremolada P, Mazzoleni M, Saliu F, Colombo M and Vighi M. 2010. Field trial for evaluating the effects on honeybees of corn sown using Cruiser ® and Celest XL ® treated seeds. Bull Environ Contam Toxicol 85(3):229-234.

USEPA. 1998. Guidelines for Ecological Risk Assessment. Published on May 14, 1998, Federal Register 63(93): 26846 – 26924. [HYPERLINK "http://www.epa.gov/raf/publications/pdfs/ECOTXTBX.PDF" \h]

USEPA, 2011. Acres Planted per Day and Seeding Rates of Crops Grown in the United States. Biological and Economic Analysis Division (BEAD), Office of Pesticide Programs, United States Environmental Protection Agency.

USEPA. 2012. White Paper in Support of the Proposed Risk Assessment Process for Bees. Submitted to the FIFRA Scientific Advisory Panel for Review and Comment September 11 – 14, 2012. Office of Chemical Safety and Pollution Prevention Office of Pesticide Programs Environmental Fate and Effects Division, Environmental Protection Agency, Washington DC; Environmental Assessment Directorate, Pest Management Regulatory Agency, Health Canada, Ottawa, CN; California Department of Pesticide Regulation (available at: [HYPERLINK "http://www.regulations.gov/" \l "!documentDetail%3BD%3DEPA-HQ-OPP-2012-0543-0004" \h])

USEPA. 2016a. Updated Screening Level Usage Analysis (SLUA) Report for Clothianidin PC# 044309. Office of Pesticide Programs. Biological and Economic Analysis Division.

USEPA. 2016b. Updated Screening Level Usage Analysis (SLUA) Report for Thiamethoxam PC# 060109. Office of Pesticide Programs. Biological and Economic Analysis Division.

USEPA/PMRA/CDPR. 2014. Guidance for Assessing Pesticide Risks to Bees. Office of Pesticide Programs, United States Environmental Protection Agency, Washington, D.C.; Health Canada Pest Management Regulatory Agency Ottawa, ON, Canada California Department of Pesticide Regulation, Sacramento, CA. June 19. (available at: [HYPERLINK "http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance" \h] [HYPERLINK "http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance" \h]).

USDA. 2017. Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen.

Valdovinos-Nunez GR, Quezada-Euan JJ, Ancona-Xiu P, Moo-Valle H, Carmona A and Ruiz Sanchez E. 2009. Comparative toxicity of pesticides to stingless bees (Hymenoptera: *Apidae: Meliponini*). *J Econ Entomol* 102(5):1737-1742.

Williams, G. R.; Troxler, A.; Retschnig, G.; Roth, K.; Yanez, O.; Shutler, D.; Neumann, P.; and L. Gauthier. 2015. Neonicotinoid pesticides severely affect honey bee queens. *Sci. Rep.* **5**, 14621; doi: 10.1038/srep14621.

Wu JY, Anelli CM, and Sheppard WS. 2011. Sub-lethal Effects of Pesticide Residues in Brood Comb on Worker Honey Bee (*Apis mellifera*) Development and Longevity. *PLoS ONE* 6(2): e14720.

Zhang, Y, Liu, S, Gu, J, Song,F, Yao, X, Liu, Z. 2008. Imidacloprid acts as an antagonist on insect nicotinic acetylcholine receptor containing the Y151M mutation. *Neuroscience Letters*. 446:97– 100.